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RADIOLOGICAL DEVICES PANEL

OF THE

MEDICAL DEVICES ADVISORY COMMITTEE

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OPEN SESSION

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TUESDAY,
MAY 23, 2006

The above-entitled matter convened at 10:15 a.m. at the Holiday Inn Gaithersburg, Two Montgomery Village Avenue, Gaithersburg, Maryland, Elizabeth A. Krupinski, Ph.D., Acting Chair, presiding.

PRESENT:

ELIZABETH A. KRUPINSKI, Ph.D.	Acting Chair
JOHN D. BOURLAND, Ph.D.	Member
JUDY M. DESTOUET, M.D.	Temp. Voting Member
SCOT E. GOLDBERG, D.O., M.B.A.	Temp. Voting Member
JACQUELIN HOLLAND, R.N.C., C.R.N.P.	Consumer Rep.
BHARAT B. MITTAL, M.D.	Member
DEBORAH J. MOORE, B.S.	Industry Rep.
E. JAMES POTCHEN, M.D., J.D.	Temp. Voting Member
XIAO-HUA ZHOU, Ph.D.	Member
NANCY G. WERSTO	Executive Secretary
NANCY BROGDON	

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SOUSAN S. ALTAIE, Ph.D.
Scientific Policy Advisor, Office of In Vitro
Diagnostic Device Evaluation and Safety

THOMAS P. GROSS, M.D., M.P.H.
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Radiation Programs

PUBLIC SPEAKERS:

COLLEEN HITTLE-DENSMORE
The Anson Group, LLC, for Giotto USA

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P-R-O-C-E-E-D-I-N-G-S

10:17 a.m.

DR. KRUPINSKI: Good morning. I would like to call this meeting of the Radiological Devices Panel to order. I also want to request that everyone in attendance at this meeting sign in the attendance sheet that is available outside the door. The agenda for this meeting is also available outside the door.

I would like to announce the remaining tentatively scheduled meetings of this panel for 2006, September 12th and November 7th. Please remember these are tentative dates. You may monitor the panel website for any updated information.

I note for the record that the voting members present constitute a quorum as required by 21 CFR Part 14. At this meeting the panel will be making a recommendation to the Food and Drug Administration on an FDA initiated reclassification proposal to reclassify full field digital mammography systems. This proposed device identification does not include for consideration devices such as Computer Aided Detection Devices, CADs, or tomosynthesis.

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1 Before we begin this meeting I would like
2 to ask our distinguished panel members who have
3 generously given their time to help the FDA in the
4 matter being discussed today and other FDA staff
5 seated at this table to introduce yourself. Please
6 state your name, your area of expertise, your
7 position, your institution, and your status on the
8 panel, voting member deputized voting member, consumer
9 representative, or industry representative.

10 I am Elizabeth Krupinski from the
11 University of Arizona, Department of Radiology. I'm
12 an experimental psychologist. I do medical image
13 perception research, observer performance, and
14 evaluation in the Department of Radiology there and a
15 lot of telemedicine work as well.

16 DR. DESTOUE: I'm Judy Destouet, Chief of
17 Mammography for Advanced Radiology in Baltimore. I'm
18 in private practice. My practice performs over
19 130,000 mammograms a year as well as all aspects of
20 breast imaging and I'm a temporary voting member.

21 DR. MITTAL: I'm Bharat Mittal. I'm
22 Chairman of Radiation Oncology at Northwestern

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1 University in Chicago. My area of expertise includes
2 all aspects of radiation oncology.

3 DR. BOURLAND: I'm Dan Bourland, Associate
4 Professor and head of physics research and education
5 at Wake Forest University. I am a voting member here.
6 My area of expertise is medical physics, principally
7 in radiation oncology and imaging for radiation
8 oncology.

9 MS. BROGDON: Good morning. I'm not a
10 member of the panel. I'm Nancy Brogdon. I'm the
11 Division Director for FDA's Division of Reproductive,
12 Abdominal and Radiological Devices.

13 MS. MOORE: I'm Deborah Moore. I'm the
14 Vice President of Regulatory and Clinical Quality for
15 Windward Medical Systems. I previously was with
16 Proxima Therapeutics with a focus on radiation
17 delivery systems and oncology.

18 MS. HOLLAND: I'm Jacquelin Holland and
19 I'm an advanced practice nurse for approximately 35
20 years working in the area of cancer screening and
21 community education. I am with the James Cancer
22 Hospital at Ohio State University Medical Center. The

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1 name of my department is the Diversity Enhancement
2 Program trying to concentrate on helping the community
3 understand cancer and clinical trials. I am a
4 nonvoting Consumer Representative.

5 DR. POTCHEN: I'm Jim Potchen. I'm
6 Professor and Chairman of Radiology at Michigan State
7 University. I have been involved in these panels for
8 some time off and on, more off than on. I teach a
9 variety of things, management, decision making. My
10 major area of expertise has been decision making in
11 medicine, law, and business, and observer performance
12 in evaluation of diagnostic modalities and technology
13 transfer is the area that I have had a major interest
14 in.

15 DR. GOLDBERG: I'm Scot Goldberg,
16 diagnostic radiologist. I work at the Women's Imaging
17 Center of Delaware in Newark, Delaware. I specialize
18 in breast imaging. I'm a voting member.

19 DR. ZHOU: I'm Andrew Zhou. I'm a
20 Professor in the Department of Biostatistics at the
21 University of Washington. My research area is to
22 develop the statistical message for evaluating

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1 diagnostic tests, particularly dealing with some of
2 the biases associated with the design in the study of
3 the diagnostic test. I'm a voting member.

4 MS. WERSTO: Good morning. My name is
5 Nancy Wersto, and I'm the Executive Secretary for the
6 Radiological Devices Advisory Panel.

7 DR. KRUPINSKI: Okay. Thank you. Ms.
8 Wersto would like to make some introductory remarks.

9 MS. WERSTO: Good morning, everyone again.
10 Before I turn the meeting over to Dr. Krupinski I'm
11 required to read two statements into the record, the
12 conflict of interest statement and the temporary
13 voting authority for our added members. FDA conflict
14 of interest disclosure statement for general matters,
15 Radiological Devices Panel of the Medical Devices
16 Advisory Committee, May 23, 2006.

17 The Food and Drug Administration, FDA, is
18 convening today's meeting of the Radiological Devices
19 Panel of the Medical Devices Advisory Committee under
20 the authority of the Federal Advisory Committee Act of
21 1972. With the exception of the industry
22 representative all members and consultants of the

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1 panel are Special Government Employees (SGEs) or
2 regular federal employees from other agencies and are
3 subject to federal conflict of interest laws and
4 regulations.

5 The following information on the status of
6 this panel's compliance with federal ethics and
7 conflict of interest laws covered by but not limited
8 to those found at 18 USC Section 208 are being
9 provided to participants in today's meeting and to the
10 public.

11 FDA has determined that members and
12 consultants of this panel are in compliance with
13 federal ethics and conflict of interest laws. Under
14 18 USC Section 208 Congress has authorized FDA to
15 grant waivers to Special Government employees who have
16 financial conflicts when it is determined that the
17 agency's need for a particular individual's services
18 outweighs his or her potential financial conflict of
19 interest.

20 Members and consultants of this panel who
21 are Special Government Employees at today's meeting
22 have been screened for potential financial conflicts

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1 of interest of their own as well as those imputed to
2 them including those of their employer, spouse, or
3 minor child related to the discussions of today's
4 meeting.

5 These interests may include investments,
6 consulting, expert witness testimony, contracts,
7 grants, CRADAs, teaching, speaking, writing, patents
8 and royalties, and primary employment. Today's agenda
9 involves a discussion regarding the reclassification
10 of full-field digital mammography systems, or FFDMs.

11 These systems would be classified as Class
12 2 special controls. Currently full-field digital
13 mammography systems are Class 3, or PMA devices.
14 Based on the agenda for today's meeting and all
15 financial interest reported by the panel members and
16 consultants, a conflict of interest waiver has been
17 issued in accordance with 18 USC Section 208(b)(3) to
18 E. James Potchen, M.D., J.D.

19 A copy of the written conflict of interest
20 waiver statement may be obtained by submitting a
21 written request to the agency's Freedom of Information
22 Office, Room 212A-30 of the Parklawn Building. A copy

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1 of this statement is also available on the web at
2 www.fda.gov/ohrms/dockets/default.htm.

3 Deborah Moore is serving as the Industry
4 Representative acting on behalf of all related
5 industry and is employed by Windward Medical, Inc.
6 This conflict of interest statement will be available
7 for review at the registration table during this
8 meeting and will be including as part of the official
9 transcript.

10 We would like to remind members and
11 consultants that if the discussions involve any other
12 products or firms not already on the agenda for which
13 an FDA participant has a personal or imputed financial
14 interest, the participants need to exclude themselves
15 from such involvement and their exclusion will be
16 noted for the record. FDA encourages all other
17 participants to advise the panel of any financial
18 relationships that they may have with any firms at
19 issue. Thank you.

20 Now for the temporary voting authority
21 statement. Pursuant to the authority granted under
22 the Medical Devices Advisory Committee Charter dated

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1 October 27, 1990, and as amended August 18, 1999, I
2 appoint the following individuals as voting members of
3 the Radiological Devices Panel for this meeting on May
4 23, 2006. Judy M. Destouet, Scot E. Goldberg, E.
5 James Potchen.

6 For the record these individuals are
7 Special Government Employees and are consultants to
8 this panel under the Medical Devices Advisory
9 Committee. They have undergone the customary conflict
10 of interest review and have reviewed the material to
11 be considered at this meeting.

12 In addition, I appoint Elizabeth A.
13 Krupinski, Ph.D., as Acting Chairperson for this
14 meeting. This memorandum was signed by Daniel G.
15 Schultz, M.D., Director, Center for Devices and
16 Radiological Health on May 2, 2006.

17 If anyone has anything to discuss
18 concerning these matters, please advise me now so that
19 we may leave the room for discussion. Okay. Dr.
20 Brogdon has a few remarks regarding panel members who
21 have recently rotated off our panel.

22 MS. BROGDON: On behalf of the Food and

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1 Drug Administration, the Division of Reproductive,
2 Abdominal and Radiological Devices, and the
3 Radiological devices Advisory Panel, I would like to
4 acknowledge Dr. Prabhakar Tripuraneni. Dr.
5 Tripuraneni is not present today because his term as a
6 voting member recently ended.

7 On April 28th the Center for Devices and
8 Radiological Health sent Dr. Tripuraneni a plaque
9 recognizing his efforts as a panel member. Today, I
10 would like to express our deepest appreciation for his
11 bringing to the panel his expertise in radiation
12 oncology and providing us with distinguished service
13 and guidance.

14 During this panel's last meeting Dr.
15 Tripuraneni made some especially insightful comments
16 on the use of a multiple-reader multiple-case study to
17 investigate intraobserver differences between chest
18 CTs and plain films. We hope that in the future we
19 will be able to have the benefit of Dr. Tripurane's
20 expertise as a panel consultant.

21 The success of this panel's work
22 reinforces our conviction that responsible regulation

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1 of medical devices depends greatly on the experience,
2 the knowledge and varied backgrounds, as well as the
3 viewpoints that are represented here. Thank you.

4 MS. WERSTO: The FDA seeks communication
5 with industry and the clinical community in a number
6 of different ways. First, FDA welcomes and encourages
7 pre-meetings with sponsors prior to all IDE and PMA
8 submissions. This affords the sponsor an opportunity
9 to discuss issues that could impact the review
10 process.

11 Second, the FDA communicates through the
12 use of guidance documents. Towards this end FDA
13 develops two types of guidance documents for
14 manufacturers to follow when submitting a Premarket
15 Notification application. One type is simply a
16 summary of the information that has historically been
17 requested on devices that are well understood in order
18 to determine substantial equivalence. The second type
19 of guidance document is one that develops as we learn
20 about new technology. FDA welcomes and encourages the
21 panel and industry to provide comments concerning our
22 guidance documents.

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1 I would now like to turn the meeting over
2 to our chairperson, Dr. Elizabeth Krupinski.

3 DR. KRUPINSKI: Thank you. Dr. Robert
4 Phillips, Chief of the Radiology Branch from the
5 Office of Device Evaluation would now like to give a
6 brief update on FDA radiology activity.

7 Dr. Phillips.

8 DR. PHILLIPS: Well, here I am again. As
9 you're aware, the panel has not met for about the last
10 year and a half. In that period of time we have had a
11 lot of interactions with manufacturers but really very
12 little on the PMA area. That is, original PMAs. What
13 we have done is approved supplements for various
14 devices. These have been in the area of CAD devices
15 primarily where manufacturers are making changes in
16 their devices or applying them to new or different
17 display systems.

18 The changes have been primarily with the
19 CAD devices that are used in mammography. The thing
20 of interest to the panel, though, is we currently have
21 a guidance that is out for comment on bone sonometers.

22 If you will recall, we have had bone sonometers as a

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1 Class 3 PMA product. These devices are devices that
2 measure bone status by means of passing an ultrasound
3 beam through the bone as opposed to what we are more
4 familiar with, bone densitometry where you pass an x-
5 ray beam through the bone.

6 The bone sonometer guidance has been out
7 for comment for the last approximately 90 days. The
8 period of review has either closed or is very close to
9 being closed. We will, in the near future, be looking
10 at the comments we received on that. It will be used
11 probably as a basis for reclassifying of bone
12 sonometry from Class 3 to Class 2. Other than that,
13 our activities have been rather routine and I'll leave
14 it at that. Are there any comments or questions?
15 Thank you.

16 DR. KRUPINSKI: Thank you, Dr. Phillips.
17 If no one has any questions, we will now proceed with
18 a presentation on the FDA's Critical Path Initiative
19 in Medical Devices by Dr. Sousan Altaie, Scientific
20 Policy Advisor from the Office of In Vitro Diagnostic
21 Device Evaluation and Safety.

22 MS. ALTAIE: Good morning. It's a

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1 beautiful day out there and I just wish the pollen
2 count was a smaller amount. You will excuse me if I
3 start coughing and hacking up here. I am the
4 Scientific Policy Advisor in the Office of In Vitro
5 Diagnostics. Also I am the Critical Path Coordinator
6 for Center for Devices.

7 Today I would like to talk to you about
8 the Critical Path Initiative, what it is, and talk
9 about the FDA interest and why FDA is interested in
10 the Critical Path Initiative and talk a little bit
11 about the critical path tools and talk about the
12 medical device areas of interest in CDRH. Then talk a
13 little bit about the device critical path projects
14 that we have in the center. Then offer you an
15 opportunity to participate in the Critical Path
16 Initiative.

17 This Critical Path Initiative is now a
18 departmental project and the Secretary of Health has
19 shown a lot of interest in it and hopefully we can get
20 some funding for it at this point. For now there is
21 no funding. We are doing what we can do as a
22 regulatory agency using our collegial interactions

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1 with the outside people on the different projects.

2 Well, Critical Path Initiative is a
3 serious attempt to make product development more
4 predictable and less costly. The Critical Path
5 Initiative covers -- if you look at the life cycle of
6 a device development or any medical product
7 development, the Critical Path skips the basic
8 research and starts with prototyping, preclinical
9 development into clinical development, and finally
10 marketing of the product. It's a journey from medical
11 product candidates to full-scale production and
12 marketing.

13 So why is FDA interested in Critical Path?

14 We are interested because we realize the significant
15 benefit of bringing innovative products to the public
16 faster because we have a unique perspective on product
17 development. We see the successes, failures, and the
18 missed opportunities because the Critical Path would
19 help us to develop guidance and standards for
20 fostering innovation.

21 We like to work together with the
22 industry, academia, patient care advocates to

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1 modernize, develop, and disseminate solutions. These
2 are tools to address scientific hurdles and device
3 development.

4 So what are these critical path tools that
5 we care so much about? These are critical path tools
6 that are methods and techniques that are used in three
7 regulatory dimensions. That is, in assessment of
8 safety, the tools predict if a potential product will
9 be harmful. In proof of efficacy, the tools determine
10 if a potential product will have medical benefits. In
11 industrialization, the tools help in manufacturing the
12 product with consistent quality.

13 When we talk about critical tools at the
14 center, we think about biomarkers, Bayesian
15 statistics, animal model biomarkers. We think about
16 computer simulations, quality assessment, protocols,
17 postmarket reporting, and anything else that the
18 public might suggest or people who are interested so
19 it's an open area for finding these tools and trying
20 to follow them and try to establish some removal
21 hurdles in device and medical product development.

22 Of course, in medical devices we have a

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1 lot of opportunities. We regulate anything from the
2 tongue depressors to band-aids to defibrillators to
3 stethoscopes to MCATs and PET CATs. We have a lot of
4 playing field to improve the product development.

5 However, I want to note that devices are
6 totally different than drugs. We deal with complex
7 components of these devices. We deal with
8 biocompatibility in durable equipment. We deal with
9 rapid production cycles, and our devices become
10 obsolete very fast. We deal with device malfunctions
11 and user errors, bench and clinical studies, quality
12 system. Regs is what we follow as opposed to drugs
13 following good manufacturing processes.

14 If we look at device safety tools,
15 biocompatibility databases are one of the ones that
16 we're looking at. We think about affects of products
17 on diseased or injured tissues when we look at the
18 device safety tools.

19 Under the device effectiveness tools, we
20 think of surrogate endpoints for cardiovascular device
21 trials. We think of computer simulation modeling for
22 implanted devices.

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1 Under device mass manufacturers or
2 industrialization of the tools, we think of practice
3 guidelines for follow-up of implanted devices. We
4 think of validating training tools for devices with a
5 known learning curve.

6 So here are examples of some critical path
7 projects that are currently under -- currently being
8 done at the Center for Devices. For validation of
9 biomarkers, we are working to qualify biomarkers for
10 personalized medicine in diagnosis and therapy as well
11 as product purity and quality. For peripheral
12 vascular stents, we are working with Stanford
13 University to develop computer models of human
14 physiology to test and predict failure even before
15 going into animal and human studies.

16 For intrapartum field diagnostic devices,
17 we are working with NIH to develop a clear regulatory
18 path with consensus from the obstetrics community. We
19 are collaborating with NIH on pharmacokinetics and
20 image guided innovations. We are working with
21 University of Stanford in San Francisco to identify
22 barriers to drug diagnostic device co-development. We

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1 are working on the pathways for statistical validation
2 of circuit markers, especially in the area of
3 cardiovascular devices.

4 We also are working with the Juvenile
5 Diabetes Research Foundation to accelerate development
6 of a closed-loop system using continuous glucose
7 sensors and insulin pumps linked by a control
8 algorithm. Our scientists in the Office of Science
9 and Engineering Laboratories are collaborating with
10 various researchers to develop animal models and
11 computer simulated virtual families to improve
12 predictions of toxic effects for medical products.

13 There is a horrendous amount of projects
14 going on in the Center. Since we don't have a budget
15 we are working on our own scientific background. We
16 are doing workshops and we are actually using the wet
17 labs outside the FDA to do all these testings that I
18 mentioned.

19 If you are interested in getting involved
20 in the Critical Path which is something that the
21 Center and the Department encourages everyone, you
22 could add to the National Critical Path Opportunities

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1 list that we have compiled. There is a list that was
2 published in April of this year and it has 76
3 opportunities. There are two documents.

4 One is a report describing the
5 opportunities and how they are categorized and where
6 we are going with these tools. The other one lists
7 the projects. You could participate by adding to this
8 list or you could pick up one of these projects and
9 actually help us accomplish that project.

10 You also can go to the webpage for the
11 Critical Path Initiative if you need more details
12 about it, and you can find a link to the critical Path
13 white paper. That is how the whole ball started
14 rolling. You can see a copy of that in that webpage.

15 Then I would like to leave you with this
16 concept. The product development has many stages,
17 parts if you like, and they are all interconnected.
18 Here at CDRH we believe in ensuring the public health
19 through the total product life cycle and we think it's
20 everyone's job. Any questions? Thank you.

21 DR. KRUPINSKI: Okay. Thank you, Dr.
22 Altaie. If no one has any questions, we will now

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1 proceed with the presentation on some of the recent
2 changes in CDRH's Condition of Approval studies by Dr.
3 Thomas Gross, Director of the Division of Postmarket
4 Surveillance in the Office of Surveillance and
5 Biometrics.

6 DR. GROSS: Good morning. I would like to
7 take a few minutes of your time to talk to you about
8 some recent changes in our Condition of Approval study
9 program. Before I do, I would like to tell you a
10 little bit about the Office of Surveillance and
11 Biometrics.

12 This is the office that is currently
13 overseeing the Condition of Approval Study program.
14 We have several functions, both pre- and postmarket.
15 On the premarket side we provide support for all
16 statistical aspects of premarket submissions, be they
17 510(k) or PMAs.

18 We also have a cadre of epidemiologists
19 who are involved in the review of original PMAs and
20 I'll say a bit more about that in a few minutes. We
21 have an interdisciplinary staff who detect signals of
22 potential public health problems through our

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1 nationwide adverse event reporting system, the medical
2 device reporting system, which gathers reports mostly
3 from manufacturers. These are mandatory reports.

4 We have another system called MedSun,
5 Medical Product Safety Network, which is comprised of
6 350 mostly hospitals throughout the United States. We
7 received from them reports of adverse events and
8 product problems. We also characterize the risk of
9 these potential public health problems and other
10 safety issues by reviewing the literature, doing
11 enhanced surveillance, de novo studies, and conducting
12 collaborative studies with academia and professional
13 societies and the like.

14 We are also responsible for coordinating
15 the center response to these high-profile safety
16 signals. We convene a panel of experts within the
17 center to deliberate these issues and provide
18 recommendations to center senior staff for action.
19 Lastly, we are responsible for interpreting the
20 Medical Device Reporting regulation, what needs to be
21 reported, and also speaking to violations of that
22 reporting requirement.

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1 Now, with regard to our Conditional
2 Approval Study program, we do have legal authority to
3 mandate manufacturers to conduct these studies if
4 provided in the regulation which states that post-
5 approval requirements can include a continuing
6 evaluation and periodic reporting on the safety,
7 effectiveness, and reliability of the device for its
8 intended use. This gives us our broad legal authority
9 to, again, ask manufacturers to conduct these studies.

10 Having said that, we decided to do an
11 internal evaluation of how well we were doing with
12 regard to oversight of these studies. Our study was
13 done, I believe, in the latter part of 2002, early
14 2003. We decided to look at original PMAs that were
15 approved from the beginning of 1998 through the end of
16 2000. All told, there were 127 PMAs. Forty-five of
17 those had Condition of Approval Study orders.

18 We did extensive review of our documents
19 to try to establish the status of these studies. All
20 told, what we found was disconcerting in the following
21 ways. We concluded that CDRH had limited procedures
22 for tracking the progress or results of these studies,

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1 that our IT and other systems were wholly deficient in
2 this regard.

3 There's huge turnover of lead reviewers
4 that resulted in lack of follow-up and continuity. Up
5 to 40 percent of those reviewers who were the lead
6 reviewers when the PMA came in the door, were no
7 longer associated with that PMA when we conducted this
8 study. Again, extreme lack of continuity.

9 Lastly, there was a lack of premarket
10 resources. Those were appropriately devoted to
11 premarket submissions and premarket review and there
12 was very little time left over for the important task
13 of overseeing these Condition of Approval studies.

14 So obviously, we decided there was a need
15 for a change, and we established goals for our
16 Condition of Approval study programs. These are broad
17 goals. Basically, what we would like to do, is have
18 these studies in place by the time the product is
19 marketed so we can gather real world safety and
20 effectiveness data as the product hits the
21 marketplace.

22 Secondly, obviously they are there to

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1 better characterize the risk/benefit profile as these
2 products are used in the real world. Of course, they
3 are there to add to our ability to make sound
4 scientific decisions.

5 So logistically what did we do? Beginning
6 January of '05, we transferred the program from the
7 premarket side of the house to the postmarket side of
8 the house, the Office of Surveillance and Biometrics.

9 We did that principally for two reasons. One, we had
10 the available resources to oversee the program. Two,
11 as I mentioned before, we have a staff of
12 epidemiologists who are expert in the design of
13 observational studies, and these conditional approval
14 studies are essentially that kind of study.

15 Also, we developed and instituted an
16 automated tracking system to make sure that we could
17 acknowledge receipt of these reports when they came in
18 the door, and we would know the status of the reports
19 throughout the period of study. That tracking system
20 was established in April of '05.

21 A bit more about the role of
22 epidemiologists. This is unique in the agency.

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1 Actually, we did a pilot study courtesy of Nancy
2 Brogdon and her staff that we piloted this concept of
3 adding epidemiologists to the PMA review team. At the
4 end of about a two-and-a-half-year pilot, we deemed it
5 very successful, and they are charged with the
6 following responsibilities.

7 Again, working in conjunction with the
8 rest of the PMA review team. They are tasked with the
9 development of the postmarket monitoring plan during
10 the premarket review process. Again, when the product
11 hits the marketplace, we will have a plan in place to
12 help best to monitor the safety and effectiveness of
13 this product not only including condition of approval
14 studies but other tools available.

15 They lead in developing well-formulated
16 postmarket questions. They lead in the design of
17 condition of approval study protocols, in the
18 evaluation study products, study progress and results
19 after approval, and they work very closely with
20 industry and the rest of the PMA review team in
21 achieving these objectives.

22 Obviously everybody has to be motivated in

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1 doing these studies, and here are some aspects that we
2 believe will help motivate good studies. First and
3 foremost, obviously, is that we have to have important
4 postmarket questions that need to be addressed in the
5 postmarket period. The essential questions have to be
6 addressed premarket.

7 There are many times residual important
8 questions that should be addressed postmarket. Those
9 need to be identified and specifically addressed via
10 good study protocol design. It has worked out between
11 us and industry. The tracking system is there to
12 acknowledge receipts of reports on a periodic basis to
13 provide feedback as to how well we think the study is
14 going.

15 In an effort to be much more transparent,
16 we plan on posting the study status of these ongoing
17 studies on the agency's website. This is currently
18 done with our drug colleagues and biologic colleagues
19 in CDER and CBER. When necessary, we may issue
20 penalties for extreme failure to conduct these studies
21 or failure to report on the status of these studies.
22 This is all laid out in draft guidance that we issued

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1 in September of last year.

2 Lastly, how does this impact the advisory
3 panel? Well, during our presentations to the advisory
4 panel we will attempt to lay out the important post-
5 approval public health questions and possible
6 approaches for panel consideration. Also, again, this
7 is laid out in the guidance that we hope to update the
8 panel, that is FDA and industry, on the status of
9 these studies as they go forward in time. Many times
10 these studies are suggested or recommended by the
11 panel.

12 That concludes my remarks. Any questions
13 I would be happy to entertain. Thank you.

14 DR. KRUPINSKI: Okay. Thank you, Dr.
15 Gross. If no one has any questions, we will now
16 proceed with a series of presentations from FDA staff
17 starting with Dr. Robert Phillips who will lead off
18 with the presentation on the background of FFDMS and
19 the regulatory history of the agency.

20 Dr. Phillips.

21 DR. PHILLIPS: Thank you again. What I
22 want to talk to you about today is to start the

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1 discussion about reclassifying full-field digital
2 mammographic systems.

3 I will cover briefly background, our
4 current situation, the device history, what premarket
5 applications we have, the basis for device approvals,
6 in other words, what basis do we use for approving
7 those PMAs, what kind of equipment problems we have
8 seen in the five years since these devices have been
9 on the market, and then what has changed that has
10 caused us to consider reclassification.

11 First of all, you are all aware of
12 film/screen systems that are used for mammography.
13 They are analog in that they use a piece of film to
14 directly convert x-rays into an image on a piece of
15 film. Digital systems are new. They came on the
16 market about early in the 1990s. They convert x-rays
17 into an electrical signal that is then translated into
18 a number. This becomes part of a numerical image
19 matrix. A computer can then process this matrix into
20 an image that is either displayed on a monitor or can
21 be printed to paper or piece of film for
22 interpretation.

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1 The devices that we are talking about now,
2 the full-field digital mammography systems are
3 intended as replacements for film/screen mammography
4 systems. Both have the same indication for use. They
5 are intended to generate mammographic images for
6 screening and diagnosis of breast cancer.

7 Now, as you heard earlier this morning
8 that I will repeat, new devices that enter the market
9 after May 28, 1976 -- and this date is important. It
10 is the date of enactment of the medical device
11 amendments to the Food, Drug, and Cosmetics Act --
12 these devices are automatically in Class 3. In other
13 words, they need Premarket Approval applications
14 approval to go on the market unless they can be shown
15 to be substantially equivalent to a device that was on
16 the market.

17 In other words, marketed prior to May 28,
18 1976, or to a legally marketed device. In other
19 words, another device that we have 510(k)'d and put on
20 the market, or they undergo a process known as de novo
21 which is a way of taking relatively simple devices and
22 getting them cleared for marketing without having to

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1 go through the PMA process.

2 Currently film screen systems of
3 mammography are classed to their pre-amendment
4 devices. In other words, film screen systems were
5 available prior to May 28, 1976. They secure
6 marketing clearance through the 510(k) process. In
7 other words, they are found substantially equivalent
8 to a predicate which is another mammographic device
9 which is already on the market.

10 Full-field digital mammography systems are
11 in Class 3. That is, they secure their marketing
12 approval through the PMA process. This is a
13 demonstration of safety and effectiveness for that
14 particular device.

15 We have been aware of digital mammography
16 systems and full-field digital mammography since about
17 the late '80s. In 1996 we had a panel meeting to
18 discuss full-field digital mammography and how we
19 would go about approving it into the market.
20 Subsequent to that meeting we had several companies
21 submit 510(k)s which use Receiver Operating
22 Characteristic (ROC) curves as their analytic method

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1 to try and show substantial equivalence to film screen
2 systems.

3 They were unable to do this primarily
4 because of the rather large intra- and inter-reader
5 variability that occurs when mammograms are read.
6 Since they could not be found substantially
7 equivalent, the pathway for getting to the market was
8 the PMA process. To date we have approved four full-
9 field digital mammography using the PMA process. We
10 also have published a guidance document that applies
11 to the Class 3 devices that spelled out what we wanted
12 to see in a PMA submission for a full-field digital
13 mammography system. This guidance was made available
14 in May of 2001.

15 As you are aware, a major study that was
16 run by the National Cancer Institute and the American
17 College of Radiology Imaging Group, ACRIN, called the
18 DMIST study, Digital Mammography Imaging Screening
19 Trial, these results were published in the New England
20 Journal of Medicine in September of last year, and
21 they are still publishing or will be publishing based
22 on more information.

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1 What are the four devices that we have
2 approved through the PMA process? The first was the
3 General Electric Senographe 2000D, and that was
4 approved January 28, 2000. The SenoScan full-field
5 digital mammography system by Fischer Imaging was
6 approved in September of 2001.

7 The Lorad Digital Breast Imager (LDBI) by
8 Hologic, Inc., was approved in March of 2002. The
9 last device that we approved was the Siemens Mammomat
10 Novation, and that was approved in August 20 of 2004.
11 Now, if you look at the slide, I also noted what type
12 of detectors they have.

13 One has a flat panel amorphous silicon
14 detector. One has an array of four charged particle
15 coupling devices. Another has an array of 12 charged
16 coupling devices. The Hologic device used an
17 amorphous selenium detector. We have covered a wide
18 range of the technologies that are available for this
19 digital transducer that are used in these devices.

20 What do we look at when we are reviewing
21 and approving a PMA? We look at three things. One,
22 the device, secondly what laboratory information we

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1 have, and thirdly, the results of clinical trials.

2 A PMA will consist of a physical
3 description of the device. It will also contain a
4 significant amount of laboratory data. These could be
5 dynamic range and sensitometric response, image
6 sharpness, and modulation transfer function, image
7 noise and exposure as the noise power spectrum,
8 detective quantum efficiency, how the automatic
9 exposure control operates, what the radiation exposure
10 is to the patient, and how the device performs when
11 scored using various phantoms used in mammographic
12 imaging.

13 In the clinical area we will see a reader
14 performance analysis. This will be an assessment of
15 sensitivity and specificity of detection on a large
16 enriched study population. This involves double
17 exposure where the same patient is exposed on the
18 analog system and then the digital system.

19 Secondly, we will see side-by-side
20 mammographic feature analysis, and this is used
21 primarily for assessing the performance of, let's say,
22 a soft image or monitor image displayed on a monitor

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1 compared to the image displayed on film or paper.
2 Then lastly, we will look at a comparison to
3 film/screen systems based on an ROC analysis.

4 What kind of problems have we had with
5 these devices since they started going on the market?
6 We had five medical device recalls. These are
7 procedures initiated by the company to correct some
8 problem that has occurred. In 2003, we had a recall
9 because the system did not meet accuracy
10 specifications required for milliamperage.

11 In 2004, we had a device that had a
12 software problem which truncated imaging. We also had
13 a situation where we were having x-ray tube overload,
14 overheating. Lastly, for 2004 we had a device that in
15 its labeling lacked technical specifications for the
16 minimum filtration and maximum line current that could
17 be used with the device.

18 Then in 2005, we had a recall for a
19 computer problem where overloading caused the
20 interruption of image acquisition. We've had three
21 reports submitted by users for problems with a device.
22 In one case it was a system that just didn't work

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1 properly, and it was completely replaced by the
2 manufacturer.

3 In another, we had procedures delayed due
4 to error readings in the system. Lastly, we had a
5 problem with the release of the compression panel
6 which caused the patient to be under compression
7 longer than necessary.

8 Now, what has changed in the last few
9 years that causes us to be here and recommend the
10 reclassification of these devices from Class 3 to
11 Class 2? First of all, we have the initial results of
12 the DMIST study. These were published, as I
13 indicated, earlier. Another speaker, a little bit
14 later will be discussing this with you.

15 Secondly, our understanding of full-field
16 digital mammography technology has improved to the
17 point where we can develop -- we feel we can develop
18 appropriate special controls that will assure adequate
19 safety and effectiveness if we were to market clear
20 these devices through the 510(k) or substantial
21 equivalence process.

22 Again, we are talking about devices that

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1 have the same Indication for Use (IFU). That is, to
2 generate full-field digital mammographic images for
3 screening and diagnosis of breast cancer.

4 Let me just spend a moment discussing the
5 reclassification process itself. You heard a little
6 bit about that this morning, but the process can be
7 initiated either by the agency when we feel there is
8 sufficient information to start the process, or by a
9 member of the public who can petition the agency to
10 initiate a reclassification procedure.

11 In either case, it requires a
12 justification for the reclassification and the
13 development of a Special Control which would allow us
14 to review the device as a Class 2 device. This
15 Special Control, in this case, is guidance on what we
16 would want to see in submission.

17 The concept and proposal is then presented
18 to an advisory panel for their recommendation, and
19 that is what we are doing today. Assuming we get a
20 positive recommendation, the proposal to reclassify
21 and the draft guidance is made available for public
22 comment by publication of notices in the Federal

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1 Register.

2 After that, the public gets a period of
3 time to comment on the proposal and the draft
4 guidance, and after we have received those comments,
5 we analyze them and make appropriate changes in the
6 guidance or process. Then, a final action
7 reclassifying the product together with a final
8 guidance would be published in the Federal Register.
9 At this point, the device would be placed into either
10 Class 1 or Class 2.

11 Now, following me you are going to have
12 several other presentations. Dr. Sophie Paquerault is
13 going to talk about the DMIST Study results. Dr.
14 Robert Jennings is going to talk about the risk to
15 health and the special controls we propose for them.
16 Dr. Richard Kaczmarek is going to talk about the role
17 of MQSA, the medical Mammography Quality Safety Act.
18 Then, we will discuss specific questions that we would
19 like the panel to answer.

20 Madam Chairman, I am finished. The next
21 speaker can be called.

22 MS. PAQUERAULT: Thank you, Dr. Phillips.

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1 As was outlined in the previous presentation, digital
2 mammography imaging screening trial provides evidence
3 for reclassification of full-field digital
4 mammographic systems. In this presentation, I will
5 give an overview of the protocol and resulting
6 conclusion.

7 The trial was funded by the National
8 Cancer Institute through the American College of
9 Radiology Imaging Network. The study was directed by
10 Dr. Etta Pisano from the University of North Carolina
11 at Chapel Hill. Dr. Pisano designed a clinical trial
12 comparing reader performance for full-field digital
13 mammography and film/screen mammography in detection
14 and characterization of breast cancer in the screening
15 setting.

16 The outcome of the trial was published
17 last September in the New England Journal of Medicine.
18 You were sent a copy of this paper. The trial
19 involved nearly 5,000 (50,000) asymptomatic women
20 presenting for screening mammography at certain free
21 clinical sites. A total of 335 women were diagnosed
22 with breast cancer. All patients participating in the

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1 study underwent both full-field digital mammography
2 and film/screen mammography acquisition.

3 Reader task were identical to the clinical
4 routine task and consist of reading mammograms using a
5 BIRADS scale providing a binary work-up
6 recommendation, and also reading breast density
7 according to the BIRADS lexicon.

8 Five digital mammographic systems were
9 used in the study, the Senoscan from Fischer Medical,
10 the Computed Radiography System for mammography from
11 Fuji, the Senograph 2000D from GE, the Digital
12 Mammography System and Selenia Full-Field Digital
13 Mammography System both from Hologic.

14 Reader performances were evaluated using
15 the area under the Receiver Operating Characteristic
16 (ROC) curves also called AUC. Secondary analyses were
17 performed using sensitivity, specificity, positive
18 predictive value. This first graph illustrates the
19 overall result among all women participating in the
20 study.

21 The dotted line represents full-field
22 digital mammography. The solid line is for film. The

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1 area under the curve (AUC) is .78 for digital. It is
2 lower for film, .74. The difference between these two
3 curves was not found to be statistically significant.

4 This is a sub-analysis of the data. Among
5 young women under the age of 50 years digital
6 achieving AUC of .84. It is statistically lower for
7 film, .69. This graph shows advantage of full-field
8 digital mammography among young women.

9 This is a summary of the study findings.
10 As reported in the paper, the reader performance for
11 digital mammography did not vary significantly from
12 that for film mammography according to race, the risk
13 of breast cancer or the type of digital machine used.

14 Also, there were no significant difference
15 in diagnosis accuracy between digital and film
16 mammography in the overall population. However, full-
17 field digital mammography was found more accurate in
18 women under the age of 50 years, women with dense
19 breasts, and premenopausal or perimenopausal women.

20 As an indication of the results of this
21 study, the call-back rate of 8.4 percent for both
22 full-field digital mammography and film/screen

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1 mammography was found similar to or lower than those
2 reported elsewhere for U.S. screening programs.

3 In summary, digital mammography and
4 film/screen mammography are equivalent. The DMIST
5 study showed advantage of full-field digital
6 mammography for a subgroup of women among the
7 population: young women, women with dense breasts,
8 and premenopausal or perimenopausal.

9 Again, DMIST provided support for
10 classification of full-field digital mammography.
11 Following this presentation, Dr. Jennings is now going
12 to present the risk to health and special control that
13 has been identified for reclassification.

14 DR. JENNINGS: There's a formal context
15 that we consider when we look at the issue of
16 reclassification. We identify the risk to health
17 presented by the device and then we look at the
18 measures that are available for mitigating these risks
19 and then ask the panel to decide whether the
20 mitigations are adequate to control the risks in a way
21 that gives us assurance that we'll have a safe and
22 effective device using a 510(k) process rather than

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1 PMA.

2 The risks to health are essentially the
3 same ones we have with screen/film systems, the
4 possibility of misdiagnosis either false/negative or
5 false/positive, image retakes due to loss of data
6 during acquisition or archiving due to positioning
7 problems.

8 You might expect to see incorrect exposure
9 here. We don't expect that to be an issue with
10 digital systems because of their dynamic range.
11 Certainly x-ray exposure, excessive breast
12 compression, electric shock, and infection or skin
13 irritation due to the compression.

14 The methods that we can use to mitigate
15 the risks involve Special Controls. The biggest one
16 is the guidance document. That will be the major
17 thing that I'll be talking about today. Manufacturers
18 also have access to voluntary standards that they can
19 comply with. There are other Special Controls. As
20 you heard about earlier, Quality System Regulations
21 (QSRs) which in the device arena take the place of
22 GMPs.

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1 You have already heard that there's a PMA
2 guidance document. We are in the process of
3 developing a 510(k) guidance. There's a general
4 software guidance document that is already available.
5 There will be a separate guidance for accessories,
6 namely review work stations. That is also under
7 development.

8 This slide should look somewhat similar to
9 the one that Bob Phillips showed. What we are
10 proposing for the 510(k) clearance, is a physical
11 device description, physical laboratory data which
12 would be similar again to the PMA guidance with some
13 differences. Namely, since we are going to be using
14 substantial equivalence, we will be comparing
15 performance of these devices to some other previously
16 cleared device.

17 There will be more comprehensive
18 evaluation of AUC systems. I'll explain where that
19 comes from in a bit. More extensive phantom scoring.
20 Then the big difference which we feel goes a long way
21 towards our goal of least burdensome approach to
22 device clearance is that we will use instead of a

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1 large clinical trial simply reader evaluation of
2 clinical films as is done in the ACR accreditation
3 process. Finally, we will use appropriate labeling as
4 another method of informing users about the
5 performance of the device.

6 In the area of imaging performance we will
7 be asking for the same kinds of things, sensitometry,
8 issues of dynamic range linearity, temporal affects
9 which affect some of these digital devices, image
10 sharpness as expressed by the modulation transfer
11 function, image noise as a function of exposure
12 expressed in terms of the noise power spectrum, and
13 the derived quantity, detector quantum efficiency
14 (DQE), again as a function of exposure and spacial
15 frequency.

16 The automatic exposure control (AEC)
17 system has a new function these days both for
18 screen/film and digital systems. Namely, in addition
19 to actually controlling the exposure, in some systems,
20 at least, it can make selections of technique factors,
21 can select the anode and filter. We are interested in
22 knowing exactly what those systems do.

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1 They also are capable of operating in
2 different modes so we want to know that information
3 for all of the available modes. In addition, we want
4 to know how the AUC system control signal to noise
5 ratio (SNR) or contrast to noise ratio (CNR) is a
6 function of breast thickness. Obviously, we want to
7 know those as a function of breast thickness in AUC
8 mode.

9 We do have some preliminary data on
10 patient dose. For June of 2000 until September of
11 2003 when the agency was certifying full-field digital
12 mammo units there were 337 units cleared. During that
13 same time Government inspectors measured doses on
14 film/screen units so there is an average value
15 available. It turns out that the digital systems
16 produce about 15 percent lower dose than the film
17 screen units.

18 This is a histogram of the dose values for
19 the digital systems. You see the peak is somewhere
20 around 150. I think screen/film systems are up around
21 180 now. You also see that there's a high dose tail
22 to that curve so we do want to look at what happens

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1 with individual systems.

2 In the area of physical laboratory data we
3 have a couple of recommendations. One is that the lab
4 measurements be made by methods that are supported by
5 standards such as those that are being developed by
6 the International Electrotechnical Commission or by
7 recommendations such as those being developed by the
8 American Association of Physicists in Medicine.

9 Another recommendation that we were
10 considering is that the AUC performance result in
11 patient dose as a function of breast thickness that
12 conforms to the EUREF acceptable level. EUREF is the
13 European Reference Organization for Quality Assurance
14 and Mammography. They have two levels of performance.
15 One is called acceptable, which is the less stringent
16 level, and the other is achievable. In other words,
17 what a good facility ought to be able to do. We are
18 asking, or considering anyway asking, that the
19 performance be at least at the acceptable level as
20 defined by EUREF.

21 In the area of clinical data, and this,
22 again, is the one where we hope to make a large

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1 difference in the difficulty of getting clearance, we
2 propose that sets of patient films be evaluated by
3 CDRH staff who are trained in the evaluation of
4 clinical films for the ACR Mammography Accreditation
5 Program.

6 The ACR procedure requires only two sets
7 of films, one set of films from a patient with fatty
8 breasts and one from a patient with dense breasts. We
9 are thinking that we would like to have several sets
10 of films covering a range of patient characteristics
11 and a range of machine settings. Still, these are
12 just normal patients so the accrual of this kind of
13 data is not a major difficulty we think.

14 Just to remind you what the ACR process
15 involves: positioning, compression, exposure level,
16 contrast, sharpness, noise, and artifacts. Of course,
17 dealing with digital images, exposure and contrast can
18 be manipulated so we might redefine those as ability
19 to obtain optimal contrast or exposure.

20 In the area of device labeling we would
21 like to see the following: a detailed quality
22 assurance program, an explicit summary of the physical

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1 device description and the laboratory data, and
2 appropriate cleaning and disinfection procedure.
3 Although we can't mandate this, we think it would be a
4 good idea that the labeling recommend that each
5 clinical facility maintain an adverse event log book.

6 The voluntary standards that are
7 available, the biggest one is not here yet, but we are
8 aware that it is under development and that is a
9 generic full-field digital mammography quality
10 assurance program. If that becomes available, then
11 our recommendation in the labeling for a detailed
12 quality assurance program could be satisfied simply by
13 reference to the ACR NEMA document.

14 There are voluntary standards covering
15 electrical and mechanical performance and
16 compatibility. There are material standards and
17 biocompatibility standards available also.

18 Quality System Regulations (QSR) require
19 that all manufacturers, both foreign and domestic,
20 have a quality system that covers design, manufacture,
21 packaging, labeling, storage, installation, and
22 servicing of medical devices. In other words, it

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1 ensures that in production the devices continue to be
2 safe and effective.

3 QSRs also provide for the monitoring of
4 device problems and inspections of the operations and
5 records of device manufacturers. CDRH has the
6 authority to enforce those QSRs so we think this goes
7 a long way towards covering device safety and
8 effectiveness as well.

9 Finally, there is the Medical Device
10 Reporting (MDR) Regulation which provides an
11 independent means of obtaining information on adverse
12 events. This is a somewhat complicated summary slide
13 that simply points out the fact that the things that
14 I've mentioned apply to, in many cases, a number of
15 individual risks. At this point I guess the issue
16 becomes one of have the mitigations that we are
17 proposing do they address the risks appropriately to
18 allow us to down classify from PMA to 510(k)?

19 DR. KACZMAREK: Good morning. The
20 reclassification of the FFDM systems has important
21 consequences for the manufacturers of these devices.
22 It also has significance for the mammography

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1 facilities who are interested in using these systems.

2 What I would like to do is discuss what
3 bearing the reclassification of full-field digital
4 mammo devices would have on screening mammography.

5 I am representing the Division of
6 Mammography Quality and Radiation Programs (DMQRP)
7 which is contained within the Office of Communication
8 Education Radiation Programs.

9 We, the DMQRP, are responsible for the
10 enforcement of the Mammography Quality Standards Act
11 (MQSA) which regulates the clinical practice of
12 mammography. Although we operate under a different
13 authority, our staff works together with the Office of
14 Device Evaluation, Office of Science and Engineering
15 Labs, to try to facilitate the delivery of high
16 quality healthcare to the public.

17 The Mammography Quality Standards Act
18 (MQSA) was passed by Congress to ensure that all women
19 have access to quality mammography for the detection
20 of breast cancer in its earliest and most treatable
21 stages. FDA was charged with developing and
22 implementing MQSA regulations and interim regulations

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1 became effective in February 1994.

2 These regulations began being enforced in
3 1995 when FDA initiated an inspection program and
4 subsequently FDA issued more comprehensive final
5 regulations which became effective in April of '99.
6 The MQSA regulations which appear in 21 CFR 900 are
7 very comprehensive.

8 They established a program for the
9 accreditation and certification of all facilities
10 performing screening mammography. They also specified
11 training and credential requirements applicable to all
12 facility personnel involved in any aspect of
13 mammography: x-ray technologists, medical physicists,
14 and physicians.

15 The regulations also address requirements
16 for equipment performance and provision for periodic
17 testing of clinically used mammography systems. It is
18 this aspect, in particular, that I want to focus on
19 here today.

20 The MQSA regulations essentially are
21 oriented towards film/screen mammographic systems
22 which were considered to be state of the art for

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1 screening when the regulations were developed and was
2 the dominant technology in use at the time.
3 Manufacturers and clinical researchers had spent a
4 considerable amount of time developing and improving
5 film/screen systems to make them as patient and
6 technology friendly as possible. Also, to lower the
7 patient dose to acceptable levels and to improve the
8 image quality to the greatest degree possible.

9 The evolution of this modality and its
10 ability to provide early detection of breast cancer is
11 why x-ray screening was able to become such a vital
12 part of the MQSA. It is important to note that FDA
13 was aided in writing regulations by the fact that the
14 American College of Radiology (ACR) had developed and
15 implemented an accreditation program for mammographic
16 facilities. This was in wide use and FDA adopted many
17 of the policies and procedures of the ACR program
18 including the equipment performance QC guidelines.

19 So, although the systems were and still
20 are highly specialized, there was very broad agreement
21 about performance criteria and also what specific QC
22 testing needed to be performed. It was relatively

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1 straightforward to incorporate this into the
2 regulations.

3 However, full-field digital detectors for
4 screening were not close to being ready for clinical
5 use when the regulations were developed. The
6 statement here, which is in 900.12(e)(6) appears in
7 the Quality Standards Requirements part. It did
8 anticipate dealing with modalities other than
9 screen/film and when FFDM systems became available,
10 FDA and facilities had to consider what equipment
11 performance criteria and what QC testing would be
12 appropriate for these systems.

13 As part of the PMA process, in addition to
14 the requirements for clinical data, we at FDA have
15 drawn upon our considerable internal experience in
16 diagnostic imaging science and required manufacturers,
17 as part of the PMA process, to provide information
18 about their systems with regard to accepted digital
19 imaging metrics.

20 Each criteria have already been mentioned,
21 and this process has been very beneficial to the
22 facilities who have purchased these FFDM systems.

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1 This is because what has resulted from all this is
2 that all FFDM systems which have gone through the FDA
3 PMA process and which are in clinical use today have
4 satisfied the agency that they meet our performance
5 requirements for digital imaging technology. We now
6 have the benefit also of the large control study, the
7 DMIST study that Sophie spoke of to reflect on.

8 Accepting the experience from the clinical
9 trials and the results of the DMIST study, which can
10 be considered to have established the clinical
11 benefits of digital mammography, I want to emphasize
12 the importance of a requirement for a Quality
13 Assurance (QA) program that we are proposing, as heard
14 earlier by the earlier speakers, that this remain as
15 part of the Special Controls.

16 From our perspective, the perspective of
17 DMQRP, the Quality Control (QC) tests have provided
18 facilities with a comprehensive set of tools to ensure
19 that the equipment is operating in a manner which
20 meets the criteria which manufacturers have specified.
21 We have gone a long way toward achieving a situation
22 which is similar to screen/film mammography where both

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1 the facilities and the manufacturers are aware of the
2 essential parts that they play in providing quality
3 mammography services so we would like to continue with
4 our success in this area.

5 Those of us involved with the
6 implementation of the Mammography Quality Standards
7 Act (MQSA) would agree with what was said earlier by
8 Bob Phillips, that our understanding of FFDM
9 technology has improved to the point where we can
10 develop appropriate Special Controls so that we can
11 assure active safety and effectiveness through the
12 510(k) process.

13 I would like to say that even the proposed
14 guidance, which has been discussed, the proposed
15 requirements for the review of clinical data, the
16 discussion we have heard about how device performance
17 would be evaluated, and the inclusion of the other
18 Special Controls the Division of Mammography Quality
19 and Radiation Programs supports the reclassification.

20 Thank you.

21 DR. KRUPINSKI: Thank you, FDA staff.

22 Does the panel have any questions for the FDA?

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1 DR. ZHOU: Yes, I have a few questions
2 about the results we reported from DMIST because
3 that's the one you rely on for your recommendation.
4 One of the conclusions from that study is that the
5 film and digital mammography are equivalent.

6 When I look at the data you show us here,
7 I'm wondering that the two ROC curves you plotted, on
8 page No. 4, I think, on the slides, how that compares
9 between the film and the digital mammography ROC curve
10 changes by readers, also by the centers. I wonder
11 whether that conclusion how we depend on which reader
12 are you looking at or which center are you looking at.
13 That is one question not clear to me.

14 Also, on the conclusion from the paper, it
15 shows the digital mammography actually is better for
16 the woman under age 50, I think. In that sense,
17 actually for some population of the patients, those
18 two systems are not equivalent.

19 The third question I have is in order to
20 establish equivalency of two diagnostic tests yearly,
21 you need to establish the range in the ROC curve to
22 say the ROC curve of the two systems within the range

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1 of 0.1 that you can they are equivalent. I would like
2 to see actually somehow we perform or you perform
3 actually bioequivalency test on those two systems.

4 DR. PAQUERAULT: As you know, we are not
5 in control of the data, and it will remain in DMIST.
6 We are taking the demonstration that Dr. Etta Pisano
7 provide us via the paper and to support
8 reclassification. What was your question about the
9 ROC curve?

10 DR. ZHOU: That is the implication that,
11 let's say, if you establish equivalency of two systems
12 in some of the centers, there are 34 --

13 DR. PAQUERAULT: Thirty-three.

14 DR. ZHOU: There are 33 centers involved,
15 so maybe it's possible that in some centers they are
16 equivalent but in other centers they are not.

17 DR. PAQUERAULT: Over all, you know.

18 DR. ZHOU: That's right.

19 DR. PAQUERAULT: It's an overall study so
20 you are looking at the average and looking at it being
21 kind of small. Quite small.

22 DR. ZHOU: Yes, but if the results

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1 actually depend on centers, then that's the real issue
2 about the conclusion that the two systems are
3 equivalent.

4 DR. PAQUERAULT: That's a question you
5 should ask to the principal investigator, I guess.

6 DR. ZHOU: It would be nice to see
7 additional data.

8 DR. KRUPINSKI: I had a question as well,
9 I guess, for Bob Jennings. You said that one of the
10 control factors was that you were going to have reader
11 evaluation of clinical films. My question, I guess,
12 is do we have any idea what percentage of systems that
13 people are actually using in clinical service, what
14 percentage are actually reading from films, hardcopy,
15 and what percentage are reading softcopy? Based on
16 that answer -- well, answer that one first. Do we
17 know what percentage of soft versus hardcopy reading
18 in clinical practice now?

19 DR. JENNINGS: I don't believe we have
20 data that is well substantiated but I have heard
21 numbers like 95 percent read from softcopy.

22 DR. KRUPINSKI: Then I guess the follow-up

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1 question then is why use film for your control process
2 and shouldn't we actually be using softcopy as your
3 standard there?

4 DR. JENNINGS: That is certainly an
5 excellent question and certainly a desirable thing to
6 do. You may be aware of the fact that independent
7 manufacturers of review stations are unable to
8 properly display certain proprietary data even though
9 ostensibly it conforms to DICOM. But, yeah, if there
10 is a way to properly display the images to our
11 readers, then that certainly would simplify things and
12 I would be all for it.

13 DR. KRUPINSKI: Dan.

14 DR. BOURLAND: I'm not exactly sure who
15 can address this one but several of you have mentioned
16 that there are, for instance, performance standards
17 both for software and then digital detectors. Are
18 those mammography specific? Are they broad enough to
19 cover what is needed to be covered? Can you tell me a
20 little bit of what's in there and how those would be
21 applied to this situation?

22 DR. PHILLIPS: The software guidance is

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1 not specific to mammography. It's a general software
2 guidance. It is designed to assure that the software
3 has been developed and designed in a structured and
4 journeyman-like fashion. As you are aware, software
5 really can't be tested after the fact to assure that
6 it is safe and effective.

7 If you don't design it in an organized
8 manner and test it as you are designing it and as you
9 are developing it, what you will end up at the end is
10 something that is unreliable. The software guidance
11 is mainly designed to assure that software that we use
12 in devices is robust. The second question was --

13 DR. BOURLAND: The digital detector
14 performance standard.

15 DR. PHILLIPS: Yes, at the present time,
16 the guidance for digital detectors is generic. It's
17 for all solid-state detectors, but that is something
18 that could be addressed in our guidance if the panel
19 felt it was appropriate.

20 DR. BOURLAND: In a guidance document
21 could it include, for instance, performance
22 specifications that are lab based that, for instance,

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1 were reviewed in part and then things such as this?
2 In other words, the digital detector as well as
3 software, those are something that could be
4 incorporated either in part or by reference or as
5 appropriate?

6 DR. PHILLIPS: Right now, they are
7 incorporated by reference. If you felt -- when the
8 guidance comes out, the public, the panel, everybody
9 will have an opportunity to comment on it, and I'm
10 sure AAPM will comment as one factor. But if the
11 comments are returned to us indicating that the
12 community feels there is a need for some specific type
13 of guidance, specific to mammography in those two
14 areas, that is something that we would consider then
15 in writing the final guidance.

16 DR. KRUPINSKI: Any other questions?

17 DR. BOURLAND: So one question and maybe
18 it's an afternoon one, but impact on manufacturers.
19 Are there some thoughts on that?

20 DR. PHILLIPS: What's the nature of the
21 question? Where are you going with it?

22 DR. BOURLAND: This would be, I think, a

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1 change for manufacturers. Maybe we are waiting to
2 hear from them perhaps. Maybe they should be the ones
3 to --

4 DR. PHILLIPS: There are two things that
5 would happen. One, for the manufacturers who
6 currently have PMAs for their devices, right now,
7 whenever they make a change in their device, they are
8 obligated to submit a supplement, a PMA supplement to
9 the agency for clearance for those changes.

10 Under a 510(k), that could be done
11 internally by the manufacturer, and the only time they
12 would need to submit a new 510(k) for their device was
13 if the change that they were making had the potential
14 for significantly changing the safety or
15 effectiveness.

16 For manufacturers who are coming on the
17 market in the future, they no longer will have to go
18 through the PMA process which means they will not have
19 to do a rather extensive clinical study and do all the
20 other major background material that we ask for in a
21 PMA. Hence, the burden on them would be significantly
22 reduced, and hopefully, the time it would take to get

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1 a new product on the market would also be reduced.

2 DR. KRUPINSKI: Anything else? Okay.
3 Thank you FDA staff. If no one has any questions, we
4 will now proceed with the first of two half-hour Open
5 Public Hearing Sessions for this meeting. The second
6 half-hour Open Public Hearing Session will follow the
7 panel discussion this afternoon. Ms. Wersto will now
8 read a statement prepared for Open Public Hearings.

9 MS. WERSTO: Thank you, Dr. Krupinski.
10 Both the Food and Drug Administration and the public
11 believe in a transparent process for information
12 gathering and decision making. To ensure such
13 transparency at the Open Public Hearing Session of the
14 Advisory Committee meeting, FDA believes it is
15 important to understand the context of an individual's
16 presentation.

17 For this reason, FDA encourages you, the
18 Open Public Hearing speaker, at the beginning of your
19 written or oral statement to advise the Committee of
20 any financial relationship that you may have with the
21 sponsor, their products, and, if known, a direct
22 competitor to full-field digital mammography systems.

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1 For example, this financial information
2 may include a sponsor's payment of your travel,
3 lodging, or other expenses in connection with your
4 attendance at the meeting. Likewise, FDA encourages
5 you at the beginning of your statement to advise the
6 Committee if you do not have any financial
7 relationships. If you choose not to address this
8 issue of financial relationships at the beginning of
9 your statement, it is not -- it will not preclude you
10 from speaking. Thank you.

11 DR. KRUPINSKI: I would like to remind
12 public observers at this meeting that while this
13 portion of the meeting is open to public observation,
14 public attendees may not participate except at the
15 specific request of the chair. We can now begin the
16 first open public portion of this meeting.

17 Ms. Colleen Hittle-Densmore, Anson Group
18 for Giotto USA.

19 MS. HITTLE-DENSMORE: Good morning. Thank
20 you very much for allowing me to speak here today. I
21 must admit, though, that with the five minutes
22 provided I'm not anticipating providing you with

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1 anything different than what was presented by the FDA.
2 As a consultant I'm in, I suppose, the enviable
3 position uniquely of being a little aligned in the
4 situation with Bob Phillips and his group. A lot of
5 my comments will be just echoing the information that
6 has been presented already this morning.

7 My name is Colleen Hittle-Densmore. I am
8 managing partner of a firm called the Anson Group.
9 Today, I am here representing two different clients,
10 one the International Medica Scientifica (IMS),
11 medical device manufacturer out of Italy, and their
12 partner Giotto USA.

13 To Nancy Wersto's point, I am here today
14 as a paid consultant to those firms. Our group, the
15 Anson Group, provides regulatory and clinical
16 strategies to medical technology companies, and we
17 have significant experience in diagnostic imaging.

18 IMS, as I said earlier, is an Italian-
19 based manufacturer of digital equipment. They have
20 been in business for over 40 years and have worldwide
21 distribution of various products. Giotto USA is their
22 exclusive distributor in the United States, and my

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1 colleague, Bob Rusk, is here today representing
2 Giotto.

3 I have just put a slide in there for
4 definitions because as a FOIA when you are searching
5 on FOIA sometimes the definitions allude you so I
6 added that slide in. We have talked already this
7 morning about the similarities between full-field
8 digital and film mammography. I think Bob Phillips
9 made the point that it has a similar indication for
10 use and similar clinical populations.

11 I am referencing various technical
12 articles today, and I have those in full copies if
13 you're interested. Obviously, you are very familiar
14 with the content of those. These are similarities
15 between the two systems. If it wasn't obvious at the
16 beginning, we are supportive, obviously, of the
17 reclassification.

18 The differences between the two, I think,
19 are important, but I think they all kind of center on
20 kind of the data management aspects of the products.
21 As we have discussed earlier this morning, I think
22 those are the aspects of the products that are well

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1 suited for Special Controls. I take the doctor's
2 point from this morning about the increased detection
3 in women over 50 with dense breasts.

4 Certainly that's a challenge with the
5 substantial equivalence argument, but I would also
6 suggest that there are many submissions in the 510(k)
7 world where there are slighter various advantages for
8 that product but the limitation in your labeling
9 allows again just the substantial equivalence
10 argument.

11 I agree with Bob Phillips' report with
12 regard to recalls and adverse events. We didn't see
13 any adverse events reported by manufacturers, but only
14 a few in the user community that we felt were fairly
15 inconsequential.

16 My closing comments are about Special
17 Controls. I think when you look at ultrasound and
18 other diagnostic imaging modalities, you can see
19 examples of where Special Control reports have been
20 used very effectively to monitor the safety and
21 efficacy of various products. I would suggest that
22 putting effort into the appropriate Special Controls

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1 for full-field digital mammography would be
2 appropriate in this case. Thank you very much.

3 DR. KRUPINSKI: Thank you. We're going to
4 save questions until the end.

5 Mr. Andrew Vandergrift from Fujifilm
6 Medical Systems USA.

7 MR. VANDERGRIFF: Good morning. My name
8 is Andy Vandergrift, and I'm the National Program
9 Manager for Women's Healthcare for Fujifilm Medical
10 Systems USA. I want to thank you for allowing us to
11 make this presentation this morning.

12 Fuji manufactures the type of devices that
13 are subject to the proposed regulatory action. In
14 fact, Fuji produced the first digital radiographic
15 systems 25 years ago and has accumulated considerable
16 experience in this field. Fuji's full-field digital
17 mammography system was one of the systems proven in
18 the DMIST trial that was discussed earlier today.

19 In addition, our Fuji CR mammography
20 system is the subject of Premarket Approval
21 application, PMA, currently under review in the FDA.
22 The Radiology Devices Panel role in advising FDA on

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1 its proposed down classification of FFDM is extremely
2 important because it directly impacts diagnostic
3 decisions and women's healthcare.

4 For its down-classing recommendation FDA
5 has drawn on experience of devices FDA approved in
6 PMAs and those used in DMIST. These devices include
7 fixed array detector systems employing one of two
8 different technologies, indirect and direct detection.

9 Both have been proven clinically.

10 They also include device types consisting
11 of monolithic sheets of photostimulable phosphorous
12 which are laser scanned known as computed radiography,
13 or CR. Similar to fixed array systems, CR systems of
14 different types are available. In formulating its
15 recommendation to FDA, the panel should be aware that
16 substantial imaging performance differences, such as
17 in detector quantum frequency (DQE), as a function of
18 spatial frequency, exist among various vendors.

19 For example, although Fuji markets various
20 digital imaging systems, we only recommend the use of
21 our 50 micron system for screening mammography. We do
22 not recommend the use of our other systems for

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1 screening due to our experience in different
2 performances of these systems. These performance
3 differences have significant implications for safety
4 and effectiveness of mammography.

5 The acceptability of digital mammography
6 below a certain level of DQE has not been proven
7 compared to those commercially available devices
8 submitted at the PMA level. The identification of
9 what are acceptable DQE levels requires much greater
10 clinical investigation.

11 To conclude, there are technological
12 design and imaging performance differences within
13 fixed array FFDM. Similarly, differences exist within
14 a group of CR devices. Regardless of whether FFDM is
15 categorized as Class 3 or Class 2, any change in
16 regulation of FFDM must ensure that products reaching
17 the market have demonstrated image quality
18 performances equivalent to or better than those
19 devices whose safety and efficacy have been
20 demonstrated through extensive clinical evaluation.

21 Thank you again for allowing us to
22 present.

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1 DR. KRUPINSKI: Thank you. Ms. Eunice Lin
2 from Konica Medical Imaging.

3 MS. LIN: Madam Chairman, members of the
4 Advisory Panel, good morning. My name is Eunice Lin.
5 I am here to represent Konica Minolta Medical Imaging.
6 I'm an employee of Konica Minolta Medical Imaging. We
7 are all here today with one common goal, and that is
8 to provide the best possible healthcare services to
9 the millions of women in the U.S., specifically in the
10 area of breast cancer detection.

11 With innovations and research provided by
12 companies like Konica Minolta and many others, we are
13 closer to reaching our goal every day. The question
14 the panel is being asked today with the proposal
15 reclassification is one to which the answer to the
16 panel must be reasonably assured. The question is, is
17 it possible to demonstrate the safety and
18 effectiveness of a digital mammography system by using
19 standardized methods for measuring performance and
20 safety parameters?

21 Konica Minolta supports FDA's proposal to
22 reclassify additional mammography systems to a class 2

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1 device. Furthermore, we believe that it is possible
2 to use standardized methods to characterize the
3 performance of a mammography system. I would like to
4 tell you today about two mammography systems that
5 Konica Minolta has commercialized worldwide. The
6 first is the REGIUS 190 CR which is a computer
7 radiography system with mammography applications. The
8 second system is REGIUS PureView mammography system.

9 This is a combination of phase contrast
10 mammography and computer radiography (CR). Phase
11 contrast mammography uses an innovative approach to
12 improve breast cancer detection. It utilizes x-ray
13 refraction and modification to amplify the contrast
14 within the breast tissue, therefore making it more
15 visible for the microcalcification and making a more
16 sharp -- increasing the sharpness, as well as
17 increasing the definition and visibility of the
18 fibrils and fringes of masses.

19 I do not have enough time to tell you more
20 about the science behind this breakthrough technology.
21 I would like to share with you, however, the benefits
22 we have observed both in the laboratories and at

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1 clinical sites outside the U.S.

2 The benefits of the digital mammography
3 system have been well documented. Like other digital
4 mammography systems, both REGIUS 190 CR and REGIUS
5 PureView mammography system contribute to the overall
6 benefits of the healthcare by reducing the number of
7 retakes, by improving the contrast which is
8 particularly useful in dense breasts, by producing
9 more consistent image quality, and by making data more
10 available electronically.

11 Specifically, the REGIUS 190 mammography
12 system also offers high resolution among its kind at
13 43 points by micron. Also, REGIUS PureView
14 mammography system offers more benefits due to the age
15 affect and magnification process. These benefits
16 include: high special resolution of 20 by micron,
17 improved sharpness from age affect, and reduced noise.

18 To assess the performance of a digital
19 mammography system, many data are gathered in the
20 laboratories prior to testing it on clinical patients.
21 I list some of them here as you have seen earlier
22 during the FDA presentation. As it was also

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1 indicated, many of these tests have been well
2 established and were accepted as industry standard,
3 and organizations such as IEC are including some of
4 these as part of the evaluation for digital
5 mammography system. Some of this has also been
6 included in the FDA guidance document.

7 We believe that clinical studies are not
8 necessary and, furthermore, as seen in the DMIST trial
9 and other PMA publication studies that we observe,
10 that the clinical studies validate the data, the
11 scientific measurements. However, they do not add
12 additional information to the performance of the
13 systems.

14 I show you two examples of a physical test
15 that we have measured in our laboratories, and you can
16 see the red dotted line there represents the computer
17 radiography system performance and the blue lines are
18 representing the phase contrast mammography PureView
19 image. The one on the left is a sharpness
20 measurement, and that is represented on our MTF curve.
21 The one on the right is the noise power spectrum which
22 measures the noise and the image. Both of these have

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1 been alluded to by FDA earlier.

2 Another physical test is a phantom test.
3 For this test we used a standard ACR 156 phantom for
4 subjective evaluation and comparison of multiple
5 mammography system. This test was done by one of our
6 clinical sites in Japan. As you can see, across the
7 board, most of these systems performed pretty
8 equivalently.

9 The test was done using two types of
10 film/screen combinations, a computer radiography
11 system, 50 micron computer radiography system, a flat
12 panel detection system, and PureView mammography
13 system. As you can see, the total scoring here that
14 PureView mammography system actually performed pretty
15 equivalently to the best film/screen system in the
16 industry. We also notice that it outperformed all the
17 other systems in detecting masses.

18 I would like to show you an example of a
19 clinical image. On the left, we have the PureView
20 mammography system image acquired by PureView
21 mammography system. On the right, is acquired using
22 film/screen. Although the projector does not do

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1 justice to the image quality here, we can still see a
2 much visible and clearly defined and more detailed
3 fibril with sticklers up here using the PureView
4 mammography system.

5 As well as well-defined margin on the
6 fringe of this mass comparing to the formless mass
7 that you see on the film/screen. This obviously
8 presents a great deal of potential for improved image
9 cancer detection. This result also is consistent with
10 the data that we have measured in the laboratories.

11 In the preliminary observer study
12 conducted by a major university in Japan, 38 patients
13 have been examined, and we were able to observe by
14 using PureView mammography system two masses and three
15 classifications were overlooked using film/screen but
16 were picked up by the radiologist by using phase
17 contrast mammography. This study was reported in the
18 Investigative Radiology in 2005.

19 In conclusion, we believe that test data
20 provides accurate measurements for clinical
21 performance. Clinical data collected in the U.S.
22 through the DMIST trial was data from the PMA

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1 submissions that we have seen outside of the U.S. have
2 provided equivalent performance of digital mammography
3 system to film/screen. Therefore, no additional
4 clinical study is necessary.

5 Our recommendation is to support the
6 reclassification of digital mammography system which
7 we believe will provide healthcare professionals in
8 the U.S. rapid access to new technologies that are
9 already available to their overseas counterparts. It
10 will accelerate improvement in healthcare for the
11 millions of women in the U.S. We fully support the
12 use of physical tests recommended by FDA to form a
13 basis for the 510(k) device evaluation. Thank you.

14 DR. KRUPINSKI: Thank you. Last
15 representative, Dr. John Sandrik from GE Healthcare.

16 DR. SANDRIK: Good morning. I am John
17 Sandrik. I am an employee of and a stockholder in the
18 GE Company. I fully expect that they are going to pay
19 for my travel expenses today. I want to thank the
20 organizers of the meeting for giving us the
21 opportunity to offer some comments on the
22 reclassification of full-field digital mammography or

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1 FFDM.

2 From the time of its introduction in 2000,
3 FFDM has been shown to provide effectiveness
4 equivalent to screen/film mammography for both the
5 screening and diagnosis of breast cancer. This has
6 been demonstrated in the clinical studies performed to
7 develop PMA submissions as well as those done after
8 the device has entered the market.

9 In the most extensive study performed to
10 date, the ACRIN DMIST, the diagnostic performance of
11 FFDM was again shown to be similar to screen/film
12 mammography when considering the entire population of
13 women in the study. However, FFDM demonstrated
14 significantly better performance for particular
15 subgroups of the study.

16 One of the concerns regarding device
17 reclassification is demonstration of reasonable safety
18 and effectiveness. As mentioned, many studies have
19 demonstrated effectiveness of FFDM at least equivalent
20 to that of the most commonly used mammographic
21 modality screen/film mammography.

22 At this time, we have had over six years

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1 of clinical experience using FDA approved systems, and
2 just over 10 percent of the systems in use at MQSA-
3 certified facilities are FFDM systems. From the point
4 of view of safety, there are many technical and
5 clinical similarities between digital and screen/film
6 systems which is a Class 2 device. We expect that
7 sufficient data are available to verify the safety and
8 effectiveness of FFDM.

9 Another concern for reclassification is
10 the availability of Special Controls. An FDA guidance
11 document has been published for Premarket Applications
12 for digital mammography systems and we recommend that
13 this guidance remain in effect, perhaps modified as
14 suggested earlier, but we basically support the
15 guidance.

16 Clinical data should be acquired on the
17 product proposed for entry into the market. The
18 certification and accreditation programs of the MQSA
19 not only provide for oversight of the practice of
20 mammography but might also serve as a source of data
21 on device performance. Mammography has a long history
22 of the application of quality assurance both through

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1 voluntary programs and MQSA mandatory programs.

2 With regard to devices, every FFDM unit is
3 operated under an FDA approved quality control plan
4 developed by the image receptor manufacturer as part
5 of the PMA submission. Data on the application of
6 these, as well as a more generic QC plan, were
7 gathered as part of the ACRIN DMIST.

8 NEMA, the National Electrical
9 Manufacturers Association, has developed standard QC
10 planned templates for displays and printers used with
11 FFDM systems. These templates are intended for use by
12 manufacturers of these devices to ensure that all
13 components of an FFDM system are covered by a QC plan.

14 As it has done in the past for screen/film
15 mammography, the American College of Radiology is also
16 developing QC plan for digital mammography. We do not
17 say that the task is accomplished, but we do believe
18 that sufficient data are available to proceed.

19 GE Healthcare supports the
20 reclassification of FFDM from Class 3 to Class 2. The
21 evidence to date does not suggest that any regulatory
22 purpose is being served by retaining FFDM in Class 3.

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1 We suggest that the principle of the least burdensome
2 approach be applied to the case of FFDM
3 reclassification. We have no doubt that advances are
4 yet to be made in digital mammography. We believe
5 that patients will more readily benefit from these
6 advances if they can be brought to market in a more
7 timely manner. I will be available if you have any
8 questions later. Thank you.

9 DR. KRUPINSKI: Okay. Thank you. Does
10 the panel have any questions for these speakers?
11 Okay. Is there anyone else who would like to present
12 to the panel? Please raise your hand and come forward
13 to the microphone. Please identify yourself and tell
14 of any device company involvement.

15 MR. TOHKA: My name is Sami Tohka. I'm
16 employed by PLANMED, a device manufacturer from
17 Finland. I just want to briefly say regards to the
18 Panel, and I agree with the previous presentations
19 that PLANMED also supports the reclassification of
20 FFDM to Class 2 device. Thank you.

21 DR. KRUPINSKI: Thank you.

22 Again, please identify yourself and tell

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1 of any device company involvement.

2 MR. WINSOR: My name is Robin Winsor. I'm
3 the Chief Technical Officer at Imaging Dynamics. We
4 are a company that makes general x-ray digital systems
5 just now. We have development of a digital
6 mammography system underway. We hope to show work and
7 progress later in the year and get our regulatory
8 filing started later on.

9 One thing that hasn't been mentioned, and
10 just for the panel's consideration, is that by
11 declassifying down to Class 2 with all the good
12 scientific data that we've had here and the well-
13 established scientific guidelines, removing the
14 barriers-to-entry for other companies that have less
15 resources than the giants that are in digital
16 mammography today, the GEs and the Fujis and Siemens
17 and so on.

18 Smaller companies like Imaging Dynamics
19 have made a difference in availability of digital x-
20 ray in general by bringing to market innovative lower
21 cost devices. Today, my company is producing systems
22 that are now marketed in 25 countries around the world

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1 and extensively in the United States. With access to
2 market through the 510(k) system that allows us to get
3 systems on the market quicker and, most importantly,
4 to bring good quality devices to the market at much
5 lower cost.

6 Today, we have systems that are a quarter
7 to a fifth of the cost of systems produced by the
8 majors, and by reducing cost, we could not only
9 accelerate the time to market for new technology but
10 make it far more available to women in the United
11 States and around the world by making it much more
12 economical for facilities to get there. Obviously, we
13 want to have good scientific guidelines that would
14 prevent poor quality products coming on the market as
15 we have certainly seen coming out of Asia and Russia.

16 There are a number of systems that are
17 based along similar technical lines but don't have the
18 quality controls so we must maintain those controls.
19 Good established guidelines allowing innovative
20 technologies to market will improve access by the
21 economic portion which today is the largest single
22 barrier to widespread adoption of facilities. We

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1 wholeheartedly support the reclassification with
2 appropriate checks and balances for quality. Thank
3 you.

4 DR. KRUPINSKI: Anyone? Come on. Again,
5 identify yourself and any company involvement.

6 MS. RYERSON: I'm Carol Ryerson. I'm
7 Director of Regulatory and Clinical Affairs for
8 Eastman Kodak Company. Our company has brought to the
9 worldwide market products for radiology and
10 improvements in technology specifically for women's
11 health and mammography for over 100 years. We have
12 progressed in also bringing to market not just the
13 traditional screen film products but also products in
14 the digital radiography area and some specific to
15 mammography.

16 We do support the down classification for
17 digital mammography products. We think that the
18 experience that we and other manufacturers have had
19 with a variety of products in the digital area for
20 mammography applications supports the down
21 classification and making that technology available to
22 medical practice.

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1 We do have a long history of developing
2 products using quality assurance methods and using
3 standards. We do think it's the right time for the
4 panel to be considering such a down classification for
5 digital mammography.

6 DR. KRUPINSKI: Is there anyone else? Any
7 final questions from the panel? Okay. Before we
8 adjourn for lunch, I would like to remind you that the
9 open committee deliberations will resume in one hour
10 at 1:15 in this room.

11 (Whereupon, at 12:17 p.m. off the record
12 for lunch to reconvene at 1:29 p.m.)

13 DR. KRUPINSKI: Good afternoon. Sit down,
14 now. I would now like to call the meeting back to
15 order. Remind public observers of the meeting that
16 while this portion of the meeting is open for public
17 observation, public attendees may not participate
18 unless specifically requested to do so by the Chair.
19 We will now continue with the Panel's general
20 discussion after which they will focus their
21 deliberations on the FDA questions. Following that,
22 we will conduct the second Open Public Hearing session

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1 to give the public an opportunity once again to direct
2 questions to either the panel or the FDA. Then Ms.
3 Shulman will guide the Panel in the completion of the
4 Reclassification Questionnaire and Supplemental
5 Satasheet Forms. We will conclude our deliberations
6 by voting on the completed forms which will formulate
7 our recommendation to the FDA.

8 The Panel may ask the FDA questions at any
9 time. We will now move to the general discussion
10 portion of the Panel's deliberations. Does anyone on
11 the panel have questions for anybody this morning, or
12 any points for discussion? At this time, we can begin
13 to focus our discussion on the FDA questions. Copies
14 of these questions are located on the tables outside
15 this conference room.

16 Question 1: Do you believe that the risks
17 to health from the device have been identified, and
18 that the mitigations for these risks are appropriate?
19 If not, what additional risks to health are presented
20 by the device? What mitigations for these risks would
21 you provide a reasonable assurance of safety and
22 effectiveness?

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1 Go ahead.

2 DR. POTCHEN: Do you want us to respond to
3 the question?

4 DR. KRUPINSKI: Yes.

5 DR. POTCHEN: I believe that the risks to
6 health from the device have been identified, and that
7 the mitigations for these risks are appropriate. Yes,
8 I think we have had very good discussion of this
9 specific issue, and I think they have been identified,
10 and I saw a magnificent list and a nice matrix, so I'm
11 satisfied.

12 DR. DESTOUET: I agree.

13 DR. MITTAL: Go ahead.

14 DR. DESTOUET: I agree. I think the risks
15 have been identified, and we understand what they are,
16 and we see that this reclassification would pose no
17 risk to human health.

18 DR. MITTAL: I also believe the risks to
19 health from this device have been identified, and I do
20 not believe there are additional risks to health from
21 this device.

22 DR. KRUPINSKI: I agree, as well, and

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1 especially the reduction and potential reduction in
2 dose is a great mitigating factor.

3 DR. ZHOU: Yes, I agree.

4 DR. GOLDBERG: I agree, as well. I was
5 also going to mention that the 15 percent decreased
6 radiation dose to patients was very important. And I
7 also agree there are no additional risks to health.

8 DR. POTCHEN: I would like to rekindle
9 that and say that there is more than I saw up there,
10 and that I think it's going to make it more effective
11 and efficient to diagnose breast cancer with this
12 increased modality because of the fact that you don't
13 have to worry about the films and a variety of other
14 things that makes it considerably more efficient and
15 effective, at least in my experience.

16 DR. KRUPINSKI: Any other comments? Okay.

17 Dr. Brogdon, in regards to questions 1, the panel
18 generally believes that the risks to health from the
19 device have been identified, and that the mitigations
20 for these risks are appropriate. The Panel has no
21 other concerns or opposing opinions. Is this
22 adequate?

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1 DR. BROGDON: Yes. Thank you.

2 DR. KRUPINSKI: Question 2: Do you
3 believe that the information to be required for 510(k)
4 clearance will be sufficient for determining
5 substantial equivalence between a new device and the
6 predicates?

7 DR. POTCHEN: Answer two. Yes.

8 DR. BOURLAND: I agree as well. And we
9 have had some discussion about the guidance document.
10 And I think the one issue was raised, for instance,
11 about what is the appropriate, so to speak, gold
12 standard type of film to use, and that perhaps digital
13 is the way to approach this. So I think there are
14 some very interesting aspects to the digital
15 components that the guidance document can be devised
16 to include some flexibility, but also important
17 aspects, relative to, in particular the digital
18 aspects.

19 DR. MITTAL: I agree with Dr. Bourland's
20 comments.

21 DR. DESTOUE: I think the 510(k) process
22 will be adequate to evaluate any additional units that

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1 come to market.

2 DR. KRUPINSKI: I agree as well.

3 DR. ZHOU: I have a small concern here.
4 Like I raised the question in the morning about the
5 variability of the accuracy among the readers. So I
6 would like to see actually if there is some evidence
7 that diagnose the accuracy of digital mammography is
8 similar than the existing film in terms of the
9 readers. So there is variability among the readers
10 because those two systems are similar, and that's the
11 data we can see from the published studies.

12 DR. KRUPINSKI: I think if we do get that
13 data, I mean, Craig Beam did a wonderful study a
14 number of years ago just on that issue, and it was
15 with film, and there was huge variability.

16 DR. ZHOU: How about the digital system?

17 DR. KRUPINSKI: He hasn't done it, but I'm
18 sure it's at least as variable as that. If it
19 decreases variability, I'm sure that would be great,
20 but I don't think anybody has done that study. I
21 mean, if the DMIST trial could give us that data, I
22 think it would be worthwhile, as well. I have doubts

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1 that it would be any more variable than film, though.

2 DR. ZHOU: Yes. If they can show it's not
3 as big as the existing one, that would be great. Then
4 I would be satisfied.

5 DR. POTCHEN: Is it appropriate to share
6 data, our experience in studying the two techniques?
7 Is that appropriate? Observer performance?

8 DR. KRUPINSKI: Yes, go ahead.

9 DR. ZHOU: I think so, yes.

10 DR. POTCHEN: Initially, if an observer
11 performance was done, it was not as good, but when
12 people gained experience it became superior very
13 rapidly. And I think the difference, initially, was
14 lack of experience. When we studied residents over
15 four years of time looking at digital and looking at
16 this, they learned much quicker with digital than they
17 do with film/screen. I think it's an improvement if
18 anything, just like we found for the others.

19 DR. ZHOU: You say --

20 DR. POTCHEN: But there was a big barrier
21 initially. People who had no experience with digital
22 at first, had trouble making the jump, but that

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1 quickly is overcome.

2 DR. DESTOUET: I think part of the problem
3 may be that you are looking at softcopy as opposed to
4 looking at film. Radiologists are trained to look at
5 hardcopy images, and there's a learning curve to look
6 at monitors.

7 DR. KRUPINSKI: And the DMIST trial was
8 with film, by the way. Everything was put into film
9 there.

10 DR. POTCHEN: But that is absolutely true.
11 The experience gleaned from softcopy now has gotten
12 so much ubiquitous across radiology that people have
13 gained the ability to do this without the error rates
14 that we had previously. It's all imperfect.

15 DR. ZHOU: But that is actually very easy
16 to see from this published data because you can have
17 an AUC or ROC curve for each reader by both systems.
18 You can just pause it and see how much variation there
19 is.

20 DR. POTCHEN: Have you done that?

21 DR. ZHOU: No, I'm talking about this
22 paper.

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1 DR. KRUPINSKI: Okay. Any other comments?

2 DR. PHILLIPS: I would just like to point
3 out that the information that FDA has available is the
4 paper that you have in front of you. We do not have
5 the raw data or access to it that supports that paper.
6 At this time we would not be able to go back and
7 analyze the individual readers in that study.

8 DR. ZHOU: Is there anyone here actually
9 familiar with this study which might answer that
10 question?

11 DR. PHILLIPS: Is that the DMIST?

12 DR. ZHOU: Yes.

13 DR. KRUPINSKI: Later on, Etta Pisano will
14 be here, so she can address that.

15 DR. MITTAL: I would like to ask a
16 question that was asked in the morning by Dr.
17 Krupinski. I think it was a very important question.
18 FDA is planning to review the hardcopies instead of
19 softcopies, and there are propriety issues as it
20 relates to reading soft films.

21 Could you approach Radiology and talk to
22 them if different vendors can come to a conclusion so

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1 that you can read the softcopies because one of the
2 advantages of digital mammography is to be able to
3 make a contrast and be able to see some of these
4 images that you may not be able to see from
5 mammography.

6 DR. KRUPINSKI: I think we can get a
7 comment on that. Introduce yourself and say how you --

8 DR. CHAKRABARTI: Kish Chakrabarti, FDA.
9 First question, you know that ACR currently are using
10 hardcopy film only because there are complexities that
11 Bob Jennings pointed out. Myself and Aldo Badano have
12 been involved with IHE. There is a handbook
13 available, and I talked to Bob Phillips already that
14 is there anyway we can accommodate that in our
15 guidance. So, definitely we are aware of that.

16 DR. POTCHEN: I would like to speak
17 strongly in favor of that so you can get comparable
18 studies across vendors, and we can do comparable
19 studies over time, so it is increasingly important as
20 we go to softcopy that we develop some standards.
21 DICOM apparently is not quite good enough to bridge
22 all the different vendors yet, but I would like to see

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1 this standardized so we can do that.

2 DR. KRUPINSKI: Any other comments with
3 regards to question No. 2? Okay. Dr. Brogdon, with
4 regards to question No. 2, the panel generally
5 believes that the information required for 510(k)
6 clearance is sufficient to determine substantial
7 equivalence between the new device and the predicates.
8 The panel had some concerns about system variability
9 and reader variability that hopefully we will be able
10 to address this afternoon. Is this adequate?

11 DR. BROGDON: Yes. Thank you.

12 DR. KRUPINSKI: Question No. 3: Do you
13 believe the materials presented support
14 reclassification of FFDM devices?

15 Jim?

16 DR. POTCHEN: Yes.

17 DR. MITTAL: I agree.

18 DR. GOLDBERG: I'll also agree, too. I
19 think we do have sufficient information here for
20 reclassification.

21 DR. BOURLAND: Agree as well.

22 DR. DESTOUET: I agree.

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1 DR. KRUPINSKI: I agree as well.

2 Andrew?

3 DR. ZHOU: Yes, I think I get satisfaction
4 from this afternoon's answers.

5 DR. KRUPINSKI: Any other comments?

6 Okay. Dr. Brogdon, in regards to question
7 No. 3, the panel generally believes that the materials
8 presented do support reclassification of FFDM devices,
9 and there are no additional concerns. Is this
10 adequate?

11 DR. BROGDON: Yes. Thank you.

12 DR. KRUPINSKI: Question No. 4. If
13 reclassified, are there any concerns that you believe
14 need to be addressed in the labeling (includes
15 direction for use, indications, and contraindications)
16 of these devices?

17 Dr. Mittal?

18 DR. MITTAL: My suggestion would be to
19 have, besides the general requirement, the special
20 requirements including the document we talked about.
21 I'm just trying to remember the name of the document.

22 DR. KRUPINSKI: There's the MQSA, the ACR.

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1 PARTICIPANT: The guidance document?

2 DR. MITTAL: The guidance document. As
3 you indicated earlier, the guidance document is in
4 that form. We would like to see the guidance document
5 implemented along with the reclassification of the
6 device from Class 3 to 2.

7 DR. KRUPINSKI: I guess my question is,
8 does that include soft copy as well as hard copy? And
9 if not, we do want them both, especially soft.

10 DR. PHILLIPS: Just a reminder. The
11 process from now on, the guidance document and the
12 reclassification process go in parallel. The next
13 step you'll see will be a notice in the Federal
14 Register announcing our intention to reclassify full-
15 field digital mammography, and also the availability
16 of a guidance document for comment. Then, that will
17 go through in parallel throughout the entire process.
18 Besides the guidance documents for full-field
19 mammography, we have another guidance for the
20 accessories, work stations, etc., that go along with
21 that. So that is essentially a package, the
22 reclassification and the two guidance documents.

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1 DR. KRUPINSKI: Great. Any other
2 comments?

3 DR. BOURLAND: Yes, I have a comment
4 concerning new things. I know that's always the
5 problem, what about new, but mostly relating to the
6 digital side. The question is, what would constitute
7 the type of, for instance, digital detector that would
8 satisfy the guidelines, basically, the guidance
9 document? Can that be written such that, do we add
10 definition to define types of detectors?

11 There will always be new detectors. The
12 x-rays will stay about the same but, for instance,
13 there could be changes there relative to beam sector,
14 for instance. So, I think these are things to think
15 about when preparing the guidance document.

16 DR. KRUPINSKI: So in a sense, how
17 different is different?

18 DR. BOURLAND: Yes, that's the issue.

19 DR. PHILLIPS: Once we go ahead and
20 reclassify these to Class 2, the 510(k) process itself
21 gives the agency a great deal of flexibility as to
22 what is equivalent, and what is not. If you go all

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1 the way back to the congressional discussion that
2 accompanied the original law, their comment on the
3 510(k) process was, it was not intended to have
4 devices that were identical, but to have devices that
5 were substantially equivalent. And the agency was not
6 only allowed but directed to use common sense in
7 making these kind of decisions. Since then, we have -
8 - I'm afraid we don't have the slide here -- but we
9 have a very laid-out process for the various types of
10 questions that we ask in a 510(k) review. Is it the
11 same indications for use? Is it the same technical
12 characteristics? Are there new issues of safety and
13 effectiveness, etc., etc., that we ask on every 510(k)
14 before we make a decision.

15 And I would just point out to you other
16 devices, such as magnetic resonance, where a great
17 deal of innovation has occurred through the 510(k)
18 process. There is a lot of judgment there in deciding
19 what is going to be an acceptable change that we can
20 still accommodate under the 510(k) process, versus
21 what is significantly different enough that we have to
22 go back to a PMA. But that is done almost on a case-

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1 by-case basis. It's very difficult to try and
2 prejudge what happens there.

3 DR. GOLDBERG: Just one question about
4 that. If the device is reclassified into a No. 2,
5 would it be under the same stipulations as film/screen
6 mammography regarding use, indication and
7 contraindication?

8 DR. PHILLIPS: If it's reclassified into
9 Class 2, the four approved devices that have PMAs
10 right now would become the predicate devices for the
11 510(k)s. So the labeling for our new device would be
12 equivalent or consistent with the labeling that
13 accompanies the four devices that have been PMAed.

14 DR. GOLDBERG: Thank you.

15 DR. KRUPINSKI: Any other comments or
16 questions? Okay. Dr. Brogdon, in regards to question
17 No. 4 the panel generally believes that there are no
18 concerns that need to be addressed in the labeling of
19 these devices other than incorporating the guidance
20 documents into their wording and everything. Is this
21 adequate?

22 DR. BROGDON: I would like to ask the

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1 staff if we have any specific questions of the panel.

2 Dr. Phillips, anything that you know of?

3 DR. PHILLIPS: I just have one
4 clarification, because this was brought up during
5 lunch. In this reclassification process, we are
6 including in the package both digital mammography, in
7 other words, the direct detectors, and computer
8 radiography (CR), the indirect detectors. We are
9 regarding both of those as being under the paradigm of
10 digital mammography.

11 DR. BROGDON: I guess we have no further
12 questions. Thank you.

13 DR. KRUPINSKI: Thank you. We will now
14 hold the second half-hour Open Public Hearing session.
15 You are reminded that the same identification
16 processes, disclosures, suggestions, and five-minute
17 maximum time limit announced for the first Open Public
18 Hearing session this morning applied to this session,
19 as well. We can now begin the Second Open Public
20 hearing session of this meeting. Margaret - or, Etta
21 Pisano.

22 DR. PISANO: I'm happy to go second.

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1 DR. KRUPINSKI: Okay. Etta Pisano, M.D.,
2 P.I., and principal author of the DMIST paper.

3 DR. PISANO: I just brought a few slides
4 to share data, and I understand there are some
5 questions so I'll try to go through these pretty
6 quickly.

7 We did find that digital had better
8 diagnostic accuracy in three subgroups. This was
9 published in the New England Journal, but there was no
10 difference in diagnostic accuracy across the entire
11 population.

12 I have the ROC curves for the entire
13 population. This is this slide. These are the AUC
14 differences. Some of this data is not in the paper.
15 This particular slide, everything in this slide is in
16 the paper, but some of the following slides are not in
17 the paper.

18 You can see that the AUC difference was
19 quite small for the entire population with a
20 nonsignificant p value, and those are the actual
21 numbers with the standard errors for digital and film.

22 These are the curves for women who are

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1 extremely dense. The solid lines are for the
2 extremely dense breasts. The dotted lines are for the
3 fatty breast. We dichotomized on the ACR four point
4 scale for density. Solid lines are for dense breasts,
5 blue being digital every slide, red being film every
6 slide. And you can see that there is a large
7 difference in the curves for the dense breasts, and
8 that the curves are closer for the fatty breasts with
9 film being slightly better than digital in the fatty
10 population but not significantly different. I'll give
11 you the raw numbers right now.

12 Here is the AUC difference for the dense-
13 breasted population including with the p value that
14 was significant. Here is the number for the fatty-
15 breasted population. The AUC difference is a negative
16 number, meaning film was slightly better than digital,
17 but p was not significant.

18 Here are the curves for women with age.
19 Solid lines were for women under 50, dotted lines for
20 women over or equal to 50. Again, a large difference
21 in the women under 50, blue always being digital, red
22 always being film. The two curves for women over 50

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1 practically overlapping.

2 These are the results for women under age
3 50, a significant p value .15 difference in area under
4 the ROC curve. For women over 50, an insubstantial
5 difference in area under the ROC curve, not
6 significant. These are the curves for women who are
7 pre- and perimenopausal, solid lines, postmenopausal,
8 dotted lines, and again blue, digital, red, film. A
9 big difference between digital and film, practically
10 overlapping in the postmenopausal group.

11 Area under the curve (AUC) difference for
12 the pre- and perimenopausal group, p value
13 significant. Here is the postmenopausal, again a
14 negative number suggesting film was ever so slightly
15 better than digital but, again, a nonsignificant p
16 value.

17 Here are the sensitivities. I'm reporting
18 these at 365 days. For the other data it was 455 days.
19 That gave us an extra 82 cancers approximately by
20 waiting out to 455 days. There were 335 cancers all
21 together in the study. You can see that these are the
22 sensitivity numbers using BIRADS scale between digital

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1 and film, so big differences 27 percent difference.
2 In women under 50, 15 percent difference. You can
3 translate these percentages.

4 Here, the specificities really did move,
5 suggesting that the reason the areas under the ROC
6 curves were different were really because we found
7 more cancers with no difference in false positives.
8 That was borne out by the actual numbers of callbacks
9 and was insubstantially different between the two
10 modalities. Positive predictive values also really
11 didn't budge.

12 Here are the number of cancers per machine
13 type which has not been published anywhere as far as I
14 can remember yet. You can see that we really don't
15 have much power for individual machines, especially
16 for Hologic and Trex, the numbers are really tiny.
17 For GE and the other machines, we do have a fair
18 amount of power, although you can see it's limited.
19 The fewer cancers, the less power. Certainly for GE,
20 we can make pretty strong statements.

21 Here I am going to show you now -- these
22 are in alphabetic order, so I have to remember which

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1 one this is. This, I believe, is Fischer. These are
2 basically overlapping. Next slide will say the
3 machine. Yes, this is the Fischer system. You can
4 see that the difference in area under the ROC curve
5 was slightly in favor of film, but really tiny
6 difference and not significant. Remember, this was
7 the second most cancers of any of the machine types.

8 This is for Fuji. Again, blue is digital,
9 red is film, and the curves are separated. Not
10 significantly so, however, but film was better than
11 digital. Again, we only had 60 cancers in the Fuji
12 population, so that is going to limit the power, but
13 you can see the ROC curve numbers. The differences do
14 overlap zero, and the p is nonsignificant, but just
15 because we only had 60 cancers.

16 Here is GE, blue over red, again digital
17 above film, but not a significant difference. Very
18 small difference in area under the ROC curve,
19 nonsignificant. I am not going to show you curves for
20 Lorad because they are so unstable with so few
21 cancers, but I will tell you, and you can take it or
22 leave it for what it's worth, you can see the width of

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1 the confidence intervals much greater as you would
2 expect with that few cancers. Same thing with
3 Hologic. Tiny little difference between the two
4 technologies, but not significant, and large
5 confidence intervals around the estimates.

6 So I am here as a private citizen today
7 not representing any one organization. Obviously,
8 with a lot of information about digital mammography,
9 and I am here today to recommend that digital
10 mammography be changed to a 510(k) from PMA.

11 I also think we could and we should
12 probably change tomosynthesis to 510(k), as well. I
13 think that probably one should treat tomosynthesis,
14 however, only that way if they can produce a two-view
15 mammogram that is a digital mammogram and then
16 additional data on top of it. In other words, if the
17 two-view mammogram is substantially equivalent to
18 another digital technology, then the additional
19 information provided by tomograms should be, if
20 anything, more helpful to radiologists.

21 So, I think I would like to see both
22 technologies classified as 510(k). So, I think that's

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1 my last slide, and I understand there are a lot of
2 questions about DMIST which I am happy to answer if I
3 can. I also am happy to answer them offline if that
4 would be helpful to the Committee. I have a lot of
5 data that I don't have in my brain, but I have in
6 another place that I could access and look at and e-
7 mail you or call you or whatever you need me to do.
8 So, I'm happy to entertain questions if you have any.

9 DR. ZHOU: So do you have the data on the
10 reader availability inaccuracy between those two
11 systems? Which system has bigger reader variability?

12 DR. PISANO: Neither. You mean digital
13 and film? They were equivalently variable. Readers
14 behave similarly for both digital and film in terms of
15 variability. The question though, I think, you know
16 of course, each reader in DMIST didn't see that many
17 cancers, so we know in terms of their callback rate,
18 etc., that they were equivalent. The readers behaved
19 very similar with both modalities, but in terms of
20 sensitivity per reader, if you think about it we don't
21 have a lot of data per reader for sensitivity. Each
22 reader only saw two or three cancers. There were 160

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1 some readers in the study.

2 DR. ZHOU: How large a variability by
3 centers?

4 DR. PISANO: We are just now looking at
5 that. We have not looked at that yet so I don't have
6 an answer to that. Remember, every center did both
7 digital and film.

8 DR. ZHOU: Yeah, so you could compare
9 them.

10 DR. PISANO: Yeah, we will, but we haven't
11 yet.

12 DR. ZHOU: Okay.

13 DR. KRUPINSKI: If the individual readers
14 were fairly consistent, you would assume that the
15 centers were probably fairly consistent as well.

16 DR. PISANO: If you are asking about
17 cross-center variability, it's possible there was
18 some, but I don't have any information about that, but
19 I don't expect there to be a difference, categorical
20 or any sort of systematic difference, between digital
21 and film given the overall results of the study.

22 Just having looked at a huge amount of

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1 data about this, I mean, obviously we only shared a
2 little bit today. That particular question, how much
3 variability there was between centers, we just now are
4 starting to look at. I don't expect a big difference.

5 DR. ZHOU: How about the gold standard
6 issue there in your study? Is the gold standard
7 unique for every patient?

8 DR. PISANO: The gold standard was biopsy
9 proof. If the patient had a biopsy, we knew about the
10 biopsy, benign or malignant. Then we had a year
11 follow-up, either a mammogram at a year or information
12 about their breast cancer status at a year. The vast
13 majority actually had a mammogram at a year.

14 DR. ZHOU: So you have two levels of a
15 gold standard so one is real gold but --

16 DR. PISANO: You mean pathology?

17 DR. ZHOU: Yes.

18 DR. PISANO: You can't do a screening
19 trial and expect everybody to have pathology because
20 only 1 percent get biopsied. The normal in a
21 screening trial -- the normal gold standard in a
22 screening trial is to watch the patients for 12

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1 months. In fact, we did more than that. We watched
2 the patients for 15 months and called it true. Most
3 screening trials only watch a patient 12 months. That
4 is pretty well accepted standard for a screening
5 trial.

6 DR. GOLDBERG: Was the 15 percent reduced
7 radiation dose to the patients regardless of the
8 breast composition whether it was dense or fatty?

9 DR. PISANO: I don't know the answer to
10 that question off the top of my head. I would have to
11 check. I believe that's true, but I don't know that
12 for sure. We were trying to match those, by the way,
13 but we could not because the machines just produced
14 the images with less radiation and the radiologist
15 didn't want to over-penetrate or overexpose the
16 breast, so we ended up doing that as part of the
17 study.

18 DR. MITTAL: How is the radiation dose
19 measured?

20 DR. PISANO: We actually use a TLD chip
21 for some subset of the patients. We imposed it in the
22 mammogram for part of a subset of our patient

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1 population. I don't remember the exact number but it
2 was multiple hundreds of patients for both digital and
3 film.

4 DR. KRUPINSKI: The details of that are
5 reported in Dr. Yaffe's paper.

6 DR. PISANO: I believe it's -- yeah, it's
7 in Medical Physics. It's been published already, I
8 believe, this month, I think.

9 DR. KRUPINSKI: Are there any other
10 questions for Dr. Pisano?

11 DR. PISANO: I just want to repeat that I
12 am willing to answer questions later if you have
13 others that you need more technical responses or more
14 detailed responses. If that is going to help you make
15 a decision, I am happy to share additional data with
16 you, so please don't hesitate to call me.

17 DR. KRUPINSKI: Thank you. Now, we will
18 go back. Margarita Zuley, M.D., American College of
19 Radiology (ACR).

20 DR. ZULEY: Hi. I'm here representing the
21 College today. I'm a private practitioner. I've been
22 a member of the College for many years, and I'm here

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1 representing over 32,000 members. The College started
2 the voluntary accreditation program for mammography in
3 1987 and was the foundation of what turned to the MQSA
4 and is now the only named accrediting body for MQSA.
5 They have been a leader in safety and quality
6 standards not only for mammography but for all of
7 radiology for a long time.

8 They strongly support the reclassification
9 of digital mammography to a Class 2 device. The
10 reasons for that are the studies that have already
11 been discussed, the ACRIN being the largest and some
12 smaller ones predating that really showing clinical
13 equivalence of the two modalities and, in some
14 instances, increased accuracy.

15 Most radiologists feel and have become
16 comfortable with, and the College feels that this
17 modality is safe and effective for patients. The
18 community has really embraced it with all these
19 studies that have come out.

20 This slide is showing from the FDA's score
21 card, the number of facilities getting digital units
22 and the number of digital units. You can see the

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1 incline in both. The digital units is red, and the
2 blue is the number of facilities. It is really
3 becoming very accepted in the community.

4 There are several reasons that the College
5 thinks this should be reclassified, and one of them is
6 patient care. It is very hard as a clinician to try
7 and recruit a patient for a study that is to fulfill a
8 PMA requirement, and double expose a patient when you
9 feel that the technology that you are trying to get
10 data for is in some respects better than the
11 technology that you are using as the gold standard.
12 That is probably the most significant reason to me, as
13 a radiologist.

14 The other more practical reasons, you
15 know, the vendors have had very slow response to
16 innovate and to change their products because
17 everything is a PMA supplement, and it requires,
18 again, double exposing the patient and requiring a lot
19 of data and reviewing those cases. It is long and
20 drawn out for them so it has been very slow for them
21 to adjust to what we feel that they need as
22 radiologists.

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1 Not only does the ACR feel that it should
2 be reclassified as a Class 2 device, but the ACR would
3 like to recommend that it be broken into two devices:
4 the first being the acquisition unit and the second
5 being processing algorithms. The separation logically
6 could occur after detector corrections are made from
7 the raw data because that would allow vendors who are
8 going to be performing processing algorithms to have a
9 very clear understanding of what they are going to be
10 starting with to provide better processing.

11 This is just a schematic showing where
12 that would happen so you acquire the raw information.
13 You detect it, do all the detector corrections and
14 then from there forward via a separate device. The
15 reason for this is primarily clinical and practical.
16 Better comparison between images.

17 I am going to show you examples of why
18 that is true. Then work flow improvements. The way
19 it is right now is that facilities that have digital
20 mammography are trying to schedule patients to go to
21 the same unit every year because the images look so
22 different coming out of the units so it is virtually

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1 impossible to run a busy facility in that kind of work
2 flow environment. But clinically is really where the
3 information is.

4 This is just some examples to show you.
5 In the screen/film world we could buy any acquisition
6 unit that we wanted and even if there were different
7 energy spectrums coming out of those units, we could
8 achieve a similar look because the screen film
9 combination and chemicals were the same. This is an
10 example of a real patient from my practice done two
11 different years in a row out of different units with
12 the same screen/film and chemical combination.

13 You can tell that is the same patient. It
14 looks very similar so my job as a radiologist reading
15 current and prior is not that hard. I am just looking
16 at the patient's tissue changing and there is no
17 technical difference between these two images.

18 This is another example of the same thing
19 yet two different units. Again, the only changes that
20 I'm looking for are in this patient, not in the
21 technology. So here is a situation. I have two
22 problems that are going on right now with digital.

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1 One is the vendors when they do change processing
2 algorithms. This is the same vendor two different
3 processing algorithms. You can see how now my job
4 just got harder because now I'm trying to not only
5 find a difference in the patient but now I have to
6 take into account the difference in technology.

7 This is another example of a different
8 vendor, two different processing algorithms applied to
9 the same patient two consecutive years in a row. Even
10 if an organization only has one unit, the radiologist
11 is at the mercy of the vendor, and every time the
12 vendor changes the processing algorithm, the
13 radiologist can never go back and use what they had
14 before. They just have to keep on the roll and keep
15 adjusting. I can't help but believe that that is
16 going to decrease our accuracy. Even though that is
17 not shown yet, it's pretty clinically apparent to me.

18 This is an example of all different
19 processing algorithms that I am dealing with right
20 now. These are all normal mammograms. These are four
21 different looks. These are all units that I have in
22 my office right now, all FDA approved pieces of

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1 equipment. Not only do I have to judge as a patient
2 moves from one unit to another, gets a new processing
3 algorithm what's changing, but every one of those is
4 normal and I have to set my threshold of number all
5 the time, every day, constantly as I read patient from
6 vendor A, patient from vendor B, patient from vendor
7 C. I am constantly adjusting my mindset.

8 This is an example of the same patient
9 done on two different units with the exact same
10 detector with different processing algorithms because
11 it's from two different vendors. You can see how
12 different that picture looks. Now I'm adjusting for
13 patient difference from year to year and vendor
14 difference from year to year.

15 Another example, different patient -- this
16 is the same patient two years in a row different from
17 the last picture I showed you. Look how different
18 that is. Very difficult to make a comparison. There
19 were some clinical issues that arose when the
20 acquisition unit was separated from the work station.
21 There were clinical issues that arose when that
22 separation was made because of incompatibility that

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1 has been worked out.

2 Our concern from the college is that now
3 we are still facing quite a bit of technical
4 differences, and it would make the radiologist's job
5 much easier and would be more safe and effective for
6 patients if you allowed the separation to occur so
7 that we as radiologists could choose one or two
8 processing algorithms, apply them to all the
9 mammograms so that the only variability we are dealing
10 with is in our patient's tissue, not in technology.
11 Thank you.

12 DR. KRUPINSKI: Thank you. Are there any
13 questions for Dr. Zuley? Thank you.

14 Our third representative, John Goble from
15 Sectra.

16 DR. GOBLE: Tough spot to follow a couple
17 of esteemed physicians who have seen more mammograms
18 than I'll ever think about. Real briefly, I'll use
19 this spot.

20 I still teach a little at Yale. One of
21 the things I talk about is that technology in the
22 medical marketplace is only acceptable for just one of

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1 three things: improve patient outcomes, reduce the
2 cost of care, or improve access of quality care to
3 under-served populations.

4 We think digital mammography has a superb
5 capability to handle all three of these aspects of
6 technology innovation in the medical marketplace and
7 believe that declassification is the right thing to do
8 to make these advantages happen.

9 We know that just as in the expedited
10 handling of anti-retrovirals in the AIDS crisis, we
11 know that we can expedite technology innovations into
12 clinical improvements. Our own company builds a
13 detector with significantly reduced radiation exposure
14 with respect to either screen/film or existing digital
15 mammography devices.

16 Certainly in Europe this has been seen as
17 a real advantage to substantially reduce radiation
18 exposure without reducing clinical effectiveness. We
19 also know of companies which are, as Rita indicated,
20 producing image processing algorithms that optimize
21 observer performance and normalize that performance
22 across multiple vendors and multiple years.

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1 We know there are high performance
2 compression algorithms that can be used to provide the
3 expertise of our mammographers into under-served
4 communities that don't have access today to the
5 quality of mammography that they should.

6 There are cancers going undetected because
7 these patients do not have access to quality care.
8 These are just a few of the many, many innovations
9 that we need to expedite into the marketplace and
10 certainly declassification into a Class 2 device will
11 help us get these things into your hands as clinicians
12 faster.

13 I won't beat this dead horse. Next
14 please. We also believe, though, that even today
15 digital mammography technology is sufficiently well
16 understood that adequate special controls may now be
17 developed and quickly. Dr. Yaffe, one of Dr. Pisano's
18 colleagues, developed quality procedures across all
19 the 30 some facilities that participated in DMIST and
20 ensured that the quality of that study stayed very,
21 very high.

22 These types of procedures exist today to

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1 maintain physical quality assurance across multiple
2 facilities. Rather than invent these things again,
3 what we recommend is that the guidance documents that
4 come from the MQSA side of things don't send this on
5 an endless ACR, AAPM, NEMA dance that will effectively
6 end up with the same thing and that is the withholding
7 of important technologies from the marketplace.

8 We would ask that the Committee recommend
9 expedited handling of this so that these technology
10 improvements can be in the hands of our clinicians
11 sooner rather than later. We also believe that
12 existing QSRs can ensure overall device compliance.
13 We think a lot of the basics are already out there,
14 what Dr. Yaffe has done as part of DMIST, other
15 standards that are already available. Let's work hard
16 and expedite these improvements in the clinical
17 practice.

18 As my father would have said, "Hey, the
19 innovation ain't done," okay? There's lots going on
20 just as it was in the early days of MR. Lots of
21 companies with lots of smart ideas are coming to the
22 marketplace and these will, in fact, result in

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1 impacting the cost of care, quality of care, access to
2 under-served populations that we ought to address.

3 So our recommendation is, of course, the
4 reclassification. Since I went through fast, I want
5 to steal one more minute. IHE is very, very
6 important. Bob can probably address this, but in the
7 initial certification process the entire imaging chain
8 was certified. There are people better qualified than
9 I to speak about this.

10 Then there was this Homer Simpson moment
11 when a patient called and came to me with my Hologic
12 stand and they had their priors on a GE disk. There
13 was this, "Duh, we've got to separate this." How can
14 I look at the priors when they come from another
15 vendor?

16 I would hope, and I address this to my FDA
17 colleagues, that the guidance document will clearly
18 separate and push whatever processing is done, à la
19 Dr. Zuley's comments, back onto the acquisition
20 station and make it simple for you as clinicians to be
21 able to compare a patient who has Fuji exam and
22 compare that to their priors who happen to be on GE or

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1 Hologic. Because of my corporate career my wife has
2 priors spread up and down the east coast.

3 Trying to compare those in a digital
4 world, fitting the films is bad enough but as Dr.
5 Zuley much more graphically than I pointed out, to
6 compare those in a digital world is a real challenge.

7 We would urge the FDA to include in their guidance
8 some of the IHE guidelines, which many of our
9 companies are actively involved in, but we would
10 encourage to push that and prioritize that so that the
11 kind of pain that Dr. Zuley is seeing on a daily basis
12 now goes away as quickly as possible.

13 That's really all the comments I had.
14 Thank you very much for your attention and we
15 appreciate the work that the Committee is doing.

16 DR. KRUPINSKI: Thank you. Are there any
17 questions for Dr. Goble? Jim.

18 DR. POTCHEN: Comments on this?

19 DR. KRUPINSKI: Yes.

20 DR. POTCHEN: I strongly support the last
21 statement made. If I see a big problem coming, for
22 those of us who read a lot of mammograms and digital

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1 mammograms, there is a wide variation of what we see.

2 Anything that we can have to make it conform so that
3 there is enough similarity that it doesn't disturb us
4 as the observer would be very helpful. This is an
5 opportunity to do so so I strongly support the last
6 speaker's comments.

7 DR. MITTAL: I have a question for Dr.
8 Pisano. I think the last presentation from ACR on
9 processing algorithm was an important issue. Could
10 you please comment on the DMIST trial? Did you see
11 that issue or anybody brought that to your attention?

12 DR. PISANO: Not as part of DMIST. It was
13 not a big issue because at that point most of the
14 vendors were relatively new. The machines were
15 relatively new and most of the sites had just
16 installed digital, and we were comparing to film. It
17 really wasn't a big issue for DMIST. It was also only
18 one time.

19 We did one screen. We weren't doing
20 repetitive screens. Although I agree with the
21 comments that have been made by the two previous
22 speakers that this is a big issue, image processing is

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1 something that as it varies from year to year can
2 really mess up an interpretive process and has to be
3 carefully watched.

4 I think it really is bad if we can't
5 compare images from one year to the next because of a
6 change in image processing. It's very confusing, and
7 I should think -- my own concern is more inter-vendor
8 variability, not being able to compare between vendors
9 because of the work station issue.

10 I think that is a real big problem. A
11 work station should have to handle each other images.
12 There should be DICOM compatibility, and they should
13 have to show them. I am not happy about that even
14 more than the image processing.

15 DR. KRUPINSKI: Were the digital printed
16 to film or read softcopy?

17 DR. PISANO: It depended on the vendor.
18 GE was all softcopy. Fuji was all hardcopy. Fischer
19 was a combination of hard and softcopy. Hologic was
20 when it was Trex Lorad, it was softcopy -- I'm sorry,
21 hardcopy, and when we switched to Hologic, it was
22 softcopy, but it stayed the same within vendor.

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1 DR. KRUPINSKI: Any other questions?

2 DR. POTCHEN: Can they put something in
3 the guidelines that would specifically address this
4 issue of the different variations in vendors from year
5 to year so we could develop some standards?

6 DR. KRUPINSKI: I think that's what part
7 of DICOM and IHE is addressing. I mean, that could be
8 incorporated in the guidelines.

9 DR. POTCHEN: Can we have that as part of
10 our recommendation if we do vote to approve this?

11 DR. KRUPINSKI: Can we put that language
12 in? Yeah, we can put that language in there.

13 DR. BROGDON: Yes.

14 DR. BOURLAND: I think the issue is a very
15 interesting one because the suggestion is to decouple,
16 for instance, processing algorithm from the digital
17 data set that it's applied to. When you have a
18 digital detector, in fact, there are differences
19 between digital detectors, different designs, for
20 instance, so there are algorithms that perhaps do a
21 few things based on the characteristics of that actual
22 detector so you have to be careful about how much can

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1 you decouple this.

2 Maybe it is processing algorithms that, in
3 fact, are related to the raw capture and the
4 particular physical characteristics for the detector,
5 and then algorithms beyond that as well so there are
6 multiple stages. More than two, if you actually go
7 through the imaging chain and count the number of
8 quanta per step.

9 DR. PISANO: I just have one comment about
10 this. In terms of proving an algorithm is useful to
11 readers or not, we're not talking about gigantic level
12 of evidence. We are talking about the number of
13 studies you have to do, and the number of readers you
14 have to do. We actually did a study in 2000 comparing
15 different image processing algorithms, and we used 27
16 mammograms with a variety of cancer/noncancer and
17 normal tissue.

18 We found statistically significant
19 differences between algorithms with, I think, eight
20 readers. It was a relatively small study using a
21 Liker scale, not using ROC performance. In other
22 words, it is not an overly burdensome thing to require

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1 the vendors to make the algorithms substantially
2 equivalent in my opinion.

3 DR. KRUPINSKI: Any other questions or
4 comments for the three?

5 DR. ZULEY: I just wanted to make a
6 clarification. I am also the clinical co-chair of the
7 mammo IHE subgroup. The IHE work that we are doing is
8 working on making sure that the mammography
9 acquisition units can display everybody's images
10 correctly. It is doing nothing about the processing
11 differences. That is out of scope for IHE.

12 DR. KRUPINSKI: Any other questions or
13 comments? Okay. If there are any individuals wishing
14 to address the panel, please raise your hand and
15 identify yourselves at this time. Please state your
16 name and your affiliation.

17 MR. UZENOFF: Hi. My name is Bob Uzenoff,
18 and I'm with Fujifilm Medical Systems. I would just
19 like to comment on the idea of making mammograms look
20 the same for ease of comparison. I am not sure if
21 what I heard before I understood correctly, but I
22 would comment that the differences in mammograms that

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1 Dr. Zuley showed between digital machines, I think
2 exist between the kinds of imaging that are done on
3 screen film currently.

4 There are different types of film,
5 different techniques that are used, different
6 radiologist preferences in what a mammogram could look
7 like from institution to institution. While a
8 clinician, I think, rightfully would like to see the
9 same kind of appearance year after year on their
10 patients, clinicians differ in what they find is a
11 comfortable film to interpret.

12 Similarly, there are different levels, and
13 we are talking about preserving innovation here in our
14 work. There are different image processing
15 algorithms. Different companies have access to
16 different technologies. Some of them are proprietary.
17 Some companies have more experience in image
18 processing in another.

19 I think you should be careful in this
20 guidance document to look at and separate areas of
21 practice which may be more properly left to
22 recommendations from the American College of Radiology

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1 to requirements for the device themself. In other
2 words, I think you want to preserve the flexibility
3 for clinicians to have the kind of image that they
4 prefer to interpret rather than to, if I could use the
5 phrase, dumb down imaging to the lowest level of
6 performance.

7 If everything has to look the same and
8 somebody has a different look, that might be a matter
9 of professional practice of whether that look is
10 something that a clinician wants to follow or not. I
11 think in whatever guidance you're asking for you want
12 to preserve the prerogative of the clinician to make
13 some of those judgments rather than to dictate that
14 they all look the same. Thank you.

15 DR. POTCHEN: I believe the Mammography
16 Standards Act require very similar looking images,
17 particularly if you send out the films to the American
18 College of Radiology for review. They have pretty
19 strict limitations as to how variable that should be.

20 Most of us have accepted a standard that is national.

21 DR. DESTOUET: Absolutely. The difference
22 from year to year is not that dramatic from patient to

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1 patient. As Dr. Potchen points out, we have specific
2 guidelines as to what the film should look like, what
3 density there should be. I think it's not as dramatic
4 as what we saw from Dr. Zuley.

5 DR. KRUPINSKI: Again, state your name and
6 affiliation.

7 MR. WINSOR: Robin Winsor, Chief Technical
8 Officer of Imaging Dynamics. I would agree with the
9 last speaker that we have to be careful on this issue
10 but some very real concerns were raised there in terms
11 of the look. As a suggestion, I would like to see the
12 approvals go through for device with software because
13 really raw data without software isn't really a
14 device, it's half a device.

15 However, our approach at Imaging Dynamics
16 is that as well as sending processed image through
17 from the device to the system on where it's going to
18 be viewed, we also store a version of the image that
19 has been data processed. We separate for definition
20 data processing from image processing.

21 Again, I'm talking at the moment in terms
22 of general radiography, but in data processing we do

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1 things like flat field corrections, pixel
2 nonuniformities and so on, things that don't change in
3 imaging a hand, a head, a hip, or breast for that
4 matter.

5 Then we layer image processing that is
6 specific to the particular view by holding onto the
7 things that are corrected, a base image that is
8 corrected for the device itself which would have no
9 value to another vendor's image processing, and taking
10 the base data that is not raw but has been properly
11 data processed and making that available if an
12 institution then wanted to apply other image
13 processing assuming the appropriate DICOM standards.
14 That could be done, and that gives us the flexibility.

15 I think to separately approve a device without its
16 associated software might be only looking at half the
17 picture.

18 MR. MARSHALL: My name is Julian Marshall.
19 I'm with R2 Technology which is being consumed by
20 Hologic Corporation. All of the prior speakers, I
21 think, have very good points, but if you go back to
22 Dr. Zuley's images, the reality is that when a patient

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1 turns up with prior mammograms from another
2 institution and the radiologist that has to read those
3 prior mammograms as part of the study did not have a
4 choice how those mammograms were produced, what image
5 acquisition unit was used, what processing was
6 applied.

7 That doctor gets precisely the films that
8 come on that CD-ROM from the site. The comparison of
9 current priors is prohibitively difficult in digital
10 because of the variance in image processing
11 algorithms.

12 Now, as Dr. Zuley suggested in her
13 diagram, if you properly define the point at which the
14 acquisition modality is done with detector corrections
15 for dead pixels and flat-fielding and so on, when you
16 define that as a standard output of an image
17 acquisition device, then it is possible to take those
18 images and regardless of the source -- we have
19 actually done this ourselves -- regardless of the
20 source, you can make one image look very much like
21 another.

22 If we fail to define that point accurately

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1 or we allow there to be a lot of slop in what the
2 definition of that point is, it will make life a lot
3 harder for the radiologist.

4 DR. KRUPINSKI: Okay. Does anyone else
5 have any comments? Any questions from the panel?
6 Okay. This concludes the second Open Public portion
7 of the meeting. We will move on to the
8 Reclassification Questionnaire and Supplemental
9 Datasheet.

10 Now that we have addressed the FDA
11 questions, we will complete the Classification
12 Questionnaire and Supplemental Datasheet. Ms.
13 Marjorie Shulman of the Office of Device Evaluation
14 will assist us as we go along.

15 After panel discussion of each question, I
16 will note our answer for each blank on the datasheet,
17 and Ms. Shulman will record it on the PC for us. We
18 will vote on the completed Questionnaire and
19 Supplemental Datasheet. It will become the Panel's
20 recommendation to the FDA. Are there any questions on
21 how we will proceed? Let's begin.

22 Ms. Shulman, will you proceed with the

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1 Questionnaire, please? We're starting with the
2 General Device Classification Questionnaire that was
3 in your notebooks. Put your name on the top one, the
4 date which is, what, the 23rd? The generic type of
5 device. Ready when you are.

6 MS. SHULMAN: Question 1: Is the device
7 life sustaining or life supporting? Go around however
8 you choose.

9 DR. KRUPINSKI: Let's just start with, I
10 guess, Dr. Bourland.

11 DR. BOURLAND: No.

12 DR. MITTAL: No.

13 DR. DESTOUET: No.

14 DR. KRUPINSKI: No.

15 DR. ZHOU: No.

16 DR. GOLDBERG: No.

17 DR. POTCHEN: No.

18 MS. SHULMAN: Thank you. Is the device
19 for a use which is of substantial importance in
20 preventing impairment of human health?

21 DR. BOURLAND: Yes.

22 DR. MITTAL: Yes.

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1 DR. DESTOUET: Yes.

2 DR. KRUPINSKI: Yes.

3 DR. ZHOU: Yes.

4 DR. GOLDBERG: Yes.

5 DR. POTCHEN: Yes.

6 MS. SHULMAN: Thank you. No. 3: Does the
7 device present a potential or reasonable risk of
8 illness or injury?

9 DR. BOURLAND: No.

10 DR. MITTAL: No.

11 DR. DESTOUET: No.

12 DR. KRUPINSKI: No.

13 DR. ZHOU: No.

14 DR. GOLDBERG: No.

15 DR. POTCHEN: No.

16 MS. SHULMAN: Thank you. No. 4: Did you
17 answer yes to any of the above questions? We did, so
18 now we may go to No. 6. Is there sufficient
19 information to establish Special Controls in addition
20 to General Controls to provide reasonable assurance of
21 safety and effectiveness?

22 DR. BOURLAND: Yes.

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1 DR. MITTAL: Yes.

2 DR. DESTOUET: Yes.

3 DR. KRUPINSKI: Yes.

4 DR. ZHOU: Yes.

5 DR. GOLDBERG: Yes.

6 DR. POTCHEN: Yes.

7 MS. SHULMAN: Thank you. Okay. If yes,
8 classify in Class 2 and go to item 7. No. 7: If
9 there is sufficient information to establish Special
10 Controls to provide reasonable assurance of safety and
11 effectiveness, identify the special controls needed to
12 provide such reasonable assurance for Class 2.

13 DR. KRUPINSKI: Do we just start with each
14 one and say yes or no to each one?

15 MS. SHULMAN: Or, if you want to start
16 with the guidance document, and then see if anyone has
17 anything to add.

18 DR. KRUPINSKI: Okay.

19 DR. BOURLAND: At this point I would have
20 guidance document.

21 DR. MITTAL: Guidance document only.

22 DR. DESTOUET: I agree.

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1 DR. KRUPINSKI: Guidance document.

2 DR. ZHOU: Guidance document.

3 DR. GOLDBERG: Guidance document.

4 DR. POTCHEN: I agree.

5 MS. SHULMAN: And is there anything to add
6 to the Special Controls?

7 DR. DESTOUET: No.

8 MS. SHULMAN: Thank you. So question 8
9 and 9, we may skip because that only has to do with
10 performance standards. Question 10: For a device
11 recommended for classification or reclassification
12 into Class 2, identify the priority for inquiring --
13 I'm sorry. Question 10 we skip. Question 11:
14 Identify the needed restrictions. Again, this is the
15 prescription question. The first one is the
16 prescription statement, and then the additional ones
17 are added on. You may answer prescription only or if
18 you have nothing else to add.

19 DR. MITTAL: I think the main issue is the
20 persons who are trained to be able to read the films
21 like you, have the second one here, that is the only
22 thing that is really applicable here.

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1 MS. SHULMAN: Okay. Thank you.

2 DR. KRUPINSKI: Is that covered -- I mean,
3 in our guidance document we are saying that MQSA must
4 be followed so is that already covered by --

5 PARTICIPANT: That covers it.

6 DR. KRUPINSKI: So we are not -- if we say
7 that, that means we are adding something additional.
8 Aren't we?

9 MS. SHULMAN: Correct.

10 DR. KRUPINSKI: So we don't check that
11 since it's already covered by MQSA.

12 MS. SHULMAN: Correct.

13 DR. POTCHEN: MQSA covers it.

14 DR. KRUPINSKI: I think we are just
15 deciding whether it's just the first box, only upon
16 the written or oral authorization basically to
17 prescription, or do we need the others checked as
18 well?

19 DR. BOURLAND: Just a clarification that
20 MQSA is within guidance document.

21 MS. SHULMAN: Correct.

22 DR. BOURLAND: Then, yes, upon

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1 prescription.

2 DR. MITTAL: I agree with Dan's comments.

3 DR. DESTOUET: I agree.

4 DR. KRUPINSKI: I agree.

5 DR. ZHOU: Agree.

6 DR. GOLDBERG: Prescription only. I
7 agree.

8 DR. POTCHEN: I agree.

9 MS. SHULMAN: Thank you. Now we can move
10 on to the Supplemental Datasheet. Again, the generic
11 type of device, the Advisory Panel of Radiology, and
12 No. 3 is the device an implant? No. Okay. Question
13 4: Indications for Use. Would you like to see them
14 again or is that agreed on the Indications for Use
15 that were presented during the panel meeting?

16 DR. DESTOUET: As presented in the panel
17 meeting.

18 DR. POTCHEN: Yes, as presented.

19 MS. SHULMAN: And everyone agrees to that?
20 Thank you. No. 5: The identification of the risk
21 to health presented by the device. Again, as
22 presented in the panel meeting or was there anything

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1 else that you would want to add?

2 DR. MITTAL: As presented.

3 MS. SHULMAN: Thank you. Question No. 6:
4 Recommended Advisory Panel classification and
5 priority. The classification is Class 2, and the
6 priority is a high, medium, and low. Basically, that
7 means how fast would you like us to work on this? To
8 move it to the top of our workload would be high,
9 medium, or low. Of course, there are no time frames
10 associated with that.

11 DR. KRUPINSKI: High.

12 DR. DESTOUET: High priority.

13 DR. POTCHEN: I would say high. Quite
14 high.

15 DR. GOLDBERG: High.

16 DR. MITTAL: Just high.

17 MS. SHULMAN: Thank you. If device is an
18 implant, life sustaining or life supporting. Let's
19 see. We answered --

20 DR. DESTOUET: General and Special
21 Controls are sufficient.

22 MS. SHULMAN: Yes, we can say General and

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1 Special Controls can handle the risks, or not
2 unreasonable risk. Is there is anything else you
3 wanted to add?

4 DR. DESTOUET: No.

5 DR. BOURLAND: No addition.

6 MS. SHULMAN: Thank you. No. 8: The
7 summary of the information including clinical
8 experience or judgment upon which classification or
9 reclassification recommendation is based on. Again,
10 you may say as presented in the panel meeting or add
11 anything else.

12 DR. DESTOUET: Yes.

13 DR. POTCHEN: As presented.

14 DR. BOURLAND: As presented.

15 MS. SHULMAN: Okay. Identification of any
16 needed restriction, Question 9: Special labeling,
17 banding. We already have the prescription use.
18 Anything that you wanted to add at this point?

19 DR. DESTOUET: No.

20 MS. SHULMAN: Thank you. No. 10 we may
21 skip because it is just for Class 1 devices. No. 11:
22 If the device is recommended for Class 2, recommended

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1 whether FDA should exempt it from Premarket
2 Notification.

3 DR. KRUPINSKI: Could you explain what
4 that means?

5 DR. MITTAL: Yeah, what does that mean?

6 MS. SHULMAN: If we exempted it from
7 premarket identification, we would not see 510(k)s for
8 it. It would still be a Class 2 device subject to
9 other Special Controls such as design controls, but we
10 would not see 510(k)s for it.

11 DR. DESTOUET: Not exempt.

12 DR. KRUPINSKI: Not exempt.

13 DR. POTCHEN: Not exempt.

14 MS. SHULMAN: Thank you. And then, if you
15 know of any -- Question 12, any other existing
16 standards to the device, assemblies, components,
17 devices materials, anything other than what was
18 presented today or anything you would like to add.

19 DR. BOURLAND: As discussed, meaning
20 software, digital detector, these types of things.

21 MS. SHULMAN: Great.

22 DR. POTCHEN: Where would we put in the

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1 idea we would like to see it standardized across --
2 somehow standardization more appropriate to the user?

3 Where would that fit in? It has been discussed, you
4 know.

5 MS. SHULMAN: We could go back and amend.

6 DR. POTCHEN: Maybe that's in the
7 guidelines. I don't know.

8 MS. SHULMAN: On the first page, you can
9 under No. 7 under 'Other' because the General Device
10 Classification Questionnaire, we have the guidance
11 document under 'Other', and you can specifically say
12 that you would like the standardization.

13 DR. POTCHEN: That's No. 7?

14 MS. SHULMAN: On the General Device
15 Questionnaire. The first one.

16 DR. ZHOU: That should be part of the
17 guidance document?

18 MS. SHULMAN: It could be part of the
19 guidance document, but if you specifically want to
20 point that out, that is where that would be added.

21 DR. POTCHEN: I would like to add it
22 because I think there is a consensus that is really

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1 relevant to making this work best for patients.

2 DR. KRUPINSKI: Standardization of a
3 default image should we call it?

4 DR. POTCHEN: Standardization so you could
5 look at multiple images from year to year, and you
6 would have something that is similar. That would be
7 nice. That is really important, I think.

8 DR. KRUPINSKI: Dr. Zuley, the
9 classification is between, you said, raw data versus
10 for presentation? Was it raw data versus for
11 presentation? Is that where the split was?

12 DR. ZULEY: Yes. After detector
13 correction but prior to any other processing. I guess
14 to the point that was made already is we are not
15 looking for one look mammogram. We are looking for
16 just the ability for the radiologist to choose a look
17 that suits them or their practice but not one standard
18 look for everybody in the country or the world.

19 DR. POTCHEN: How does that differ from
20 the standardization in MQSA already?

21 DR. ZULEY: Well, because --

22 DR. POTCHEN: We already standardized it.

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1 DR. ZULEY: The screen/film combination
2 and chemicals that I use doesn't have to be the same
3 that you use. It is just that you have to have the
4 same thing for you all through your facility. If we
5 separate them into two different devices, then we can
6 each process them differently as long as those
7 processing algorithms have some sort of quality to
8 them.

9 DR. POTCHEN: If we were to put
10 standardization under 'Other', would that meet that
11 need? Would that communicate the essence of what we
12 discussed?

13 MS. SHULMAN: It would, and then we would
14 take it back and then we could see if it would be
15 included in the guidance document or not.

16 DR. ZHOU: I don't think this is so simple
17 issue. There are a lot of technical issues here.

18 DR. BOURLAND: I think that's the
19 question, and that is we need to be careful that we
20 don't define essentially technology or limit it in
21 some fashion. I have drawn three little boxes. You
22 have data, data processing, and the question is: Is

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1 that the raw image after that? Was it the raw image
2 halfway through? Was there one more box before
3 you get to a deliverable image that then applied other
4 image processing? The question is how many boxes are
5 there, and where that line is drawn? I don't
6 necessarily disagree with the idea of having a line
7 drawn somewhere. I don't know that I could say today
8 where to put that.

9 MS. SHULMAN: Certainly, because this is a
10 recommendation, and then we'll take it back and see if
11 we can --

12 DR. BOURLAND: I think with that
13 qualification that is the thing to do.

14 DR. DESTOUET: So what do we say,
15 standardization of image processing?

16 DR. BROGDON: I've lost track of whether
17 you're discussing provisions for a guidance document
18 or whether you are seriously considering breaking this
19 one device up into two devices or more.

20 DR. KRUPINSKI: No. I think it's for the
21 guidance document. That would make things too
22 complicated I think.

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1 DR. ZHOU: I think the software is -- I
2 mean, I think I agree with one of the speakers, it's
3 part of the system so you can't standardize software
4 because some companies are better than others who
5 produce software so that should be part of it.

6 DR. POTCHEN: We have DICOM standards, and
7 we can compare images. The DICOM standards work
8 pretty well for a lot, and I have seen it work as well
9 here as I would like to see it.

10 DR. BOURLAND: And I think what this
11 suggestion is to an image which is before the DICOM
12 image, and then what is its standard?

13 DR. KRUPINSKI: So the message is being
14 taken back. Do we have to write anything down?

15 MS. SHULMAN: No, we'll read it from the
16 transcripts.

17 DR. KRUPINSKI: Okay. So that is the end
18 of the forms, and we are going to vote one more time
19 on the forms as completed as being reclassified into
20 Class 2 requiring Premarket Notification. Are there
21 any questions from the panel before we vote on the
22 completed forms? Is there a motion?

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1 DR. POTCHEN: I so move.

2 DR. MITTAL: Second.

3 DR. KRUPINSKI: It has been moved and
4 seconded that the motion to reclassify the FFDM device
5 from Class 3 into Class 2, that the Special Control
6 for digital mammography be a guidance document. All
7 in favor of the motion please raise your hand. Dr.
8 Bourland, yes.

9 DR. BOURLAND: Yes.

10 DR. KRUPINSKI: Dr. Mittal, yes.

11 DR. MITTAL: Yes.

12 DR. KRUPINSKI: Dr. Destouet.

13 DR. DESTOUET: Yes.

14 DR. KRUPINSKI: Dr. Krupinski, yes. Dr.
15 Zhou?

16 DR. ZHOU: Yes.

17 DR. GOLDBERG: Yes.

18 DR. KRUPINSKI: Dr. Goldberg, yes. Dr.
19 Potchen?

20 DR. POTCHEN: Yes.

21 DR. KRUPINSKI: Okay. All opposed? None.

22 Anyone abstaining from the vote, please raise your

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1 hand.

2 DR. BROGDON: After the vote is complete,
3 you probably ought to get comments from the Industry
4 and Consumer Representatives also.

5 DR. KRUPINSKI: Okay. Go ahead.

6 MS. HOLLAND: My comment is that I am
7 satisfied at this point that we are meeting the needs
8 of the general population with this particular
9 reclassification. I have nothing to add.

10 MS. MOORE: And I second that. I think I
11 fully support FDA's position that has been presented
12 by industry today, industry classification. I think
13 this will allow companies to innovate and bring this
14 technology available to more women. In fact, make a
15 technology that is, in fact, better in some cases.

16 DR. KRUPINSKI: Thank you.

17 MS. SHULMAN: Thank you very much.

18 DR. KRUPINSKI: Okay. The motion carried
19 seven to zero. There were no abstentions. It is the
20 recommendation of the panel that full-field digital
21 mammography systems (FFDMs) be reclassified into Class
22 2 with the guidance document to be developed for the

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1 device containing the information agreed upon today.

2 I am now going to ask each panel Voting
3 Member the reason for his or her vote starting with
4 Dr. Bourland. Or, if you just have any comments to
5 make.

6 DR. BOURLAND: Well, the answer is yes, I
7 agree with this vote. I think the level of technology
8 has been, one, developed, two, tested, and shown
9 clinical effectiveness, and that this is a means for
10 better propagational technology to the community and
11 for public health and well being.

12 DR. MITTAL: I have nothing else to add
13 except what has already been said.

14 DR. DESTOUET: The technology, as it exist
15 today, is very expensive and prohibitive for many
16 users, and if there is anything that the manufacturers
17 can do out there to give us technology that is less
18 costly but effective, it will help save women's lives.

19 DR. KRUPINSKI: I agree, and I feel that
20 by doing this reclassification we have opened it up to
21 some of the smaller companies that should be able to
22 accomplish that and reach women in rural areas by

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1 direct digital telemammography and so on.

2 DR. ZHOU: I agree. I think the evidence
3 presented to us convinced me that this device actually
4 poses equal or less risk than the previous one also
5 effective.

6 DR. GOLDBERG: I agree with the vote and
7 have nothing further to add.

8 DR. POTCHEN: I think the two major
9 reasons that I think I would favor it is that it is
10 improved care in some patients, and it decreases
11 radiation dose for all patients. I think the most
12 compelling argument given to me was that by
13 eliminating the need for subsequent PMA studies, we
14 have eliminated the need for double exposure to
15 patients undergoing those studies. That is a very
16 important concept to put forward in this type of
17 approval.

18 MS. HOLLAND: I have nothing further to
19 add.

20 MS. MOORE: Nothing further.

21 DR. KRUPINSKI: Dr. Brogdon, do you have
22 any further comments?

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1 DR. BROGDON: Nothing further. Thank you.

2 DR. KRUPINSKI: Having addressed the FDA
3 questions on the reclassification of full-field
4 digital mammography systems, the Panel has completed
5 its charge. I would like to thank the Panel for its
6 deliberations, the FDA staff and the public for their
7 comments. This meeting is adjourned.

8 (Whereupon, at 2:48 p.m. the meeting was
9 adjourned.)

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